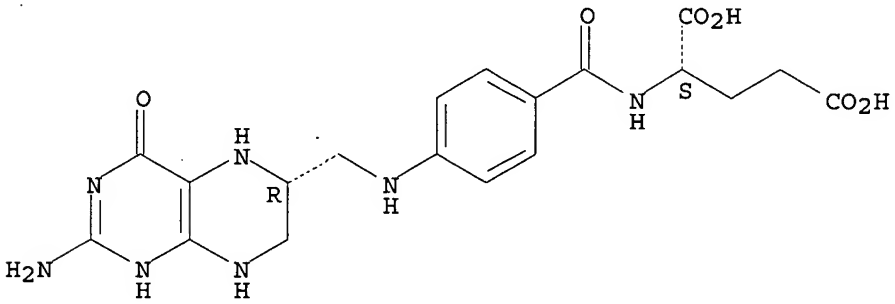
L15 ANSWER 4 OF 5 REGISTRY COPYRIGHT 2003 ACS on STN
RN 104-15-4 REGISTRY
CN **Benzenesulfonic acid, 4-methyl- (9CI)** (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN **p-Toluenesulfonic acid (7CI, 8CI)**
OTHER NAMES:
CN **4-Methylbenzenesulfonic acid**
CN **4-Toluenesulfonic acid**
CN Cyzac 4040
CN K-Cure 1040
CN Nacure 1040
CN NSC 167068
CN NSC 2167
CN **p-Methylbenzenesulfonic acid**
CN **p-Methylphenylsulfonic acid**
CN **p-Toluenesulphonic acid**
CN **p-Tolylsulfonic acid** tolyl
CN PTS 100
CN **Toluenesulfonic acid**
CN Tosic acid
AR 25231-46-3
FS 3D CONCORD
DR 402-47-1, 128739-80-0, 126033-27-0, 114213-96-6, 156627-46-2, 144647-92-7, 100901-72-2, 210357-81-6, 227313-49-7, 369371-25-5, 613262-31-0
MF **C7 H8 O3 S**
CI COM
LC STN Files: AGRICOLA, ANABSTR, AQUIRE, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, CSNB, DETHERM*, DIPPR*, EMBASE, ENCOMPLIT, ENCOMPLIT2, ENCOMPPAT, ENCOMPPAT2, GMELIN*, HODOC*, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, NIOSHTIC, PDLCOM*, PIRA, PROMT, RTECS*, SPECINFO, TOXCENTER, TULSA, ULIDAT, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: DSL**, EINECS**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)

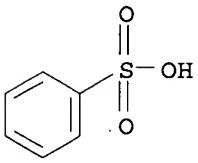
3 21 ANSWERS REGISTRY COPYRIGHT 2003 ACS on STN
IN L-Glutamic acid, N-[4-[[(2-amino-1,4,5,6,7,8-hexahydro-4-oxo-6-pteridinyl)methyl]amino]benzoyl]-, (R)-, monobenzenesulfonate (9CI)
MF C19 H23 N7 O6 . C6 H6 O3 S

CM 1

Absolute stereochemistry.



CM 2



from Miller

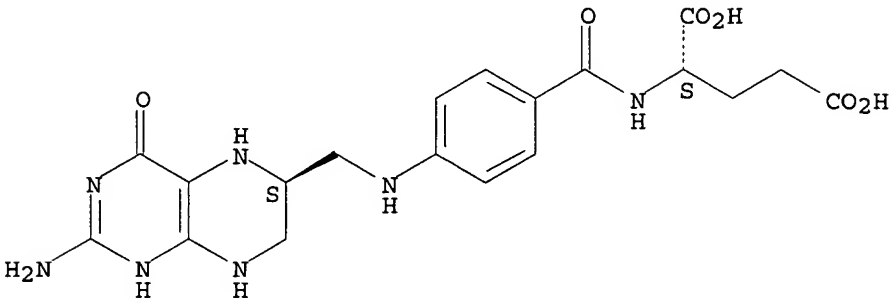
1-1 phenyl sulfonic acid

IN L-Glutamic acid, N-[4-[[(2-amino-1,4,5,6,7,8-hexahydro-4-oxo-6-pteridinyl)methyl]amino]benzoyl]-, (S)-, mono(4-methylbenzenesulfonate) (9CI)

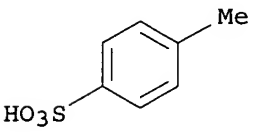
MF C19 H23 N7 O6 . C7 H8 O3 S

CM 1

Absolute stereochemistry.



CM 2



1-1 from Muller
toluene sulfonic acid

10/ 030,693

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NEWS 3	Jun 03	New e-mail delivery for search results now available
NEWS 4	Aug 08	PHARMAMarketLetter(PHARMAML) - new on STN
NEWS 5	Aug 19	Aquatic Toxicity Information Retrieval (AQUIRE) now available on STN
NEWS 6	Aug 26	Sequence searching in REGISTRY enhanced
NEWS 7	Sep 03	JAPIO has been reloaded and enhanced
NEWS 8	Sep 16	Experimental properties added to the REGISTRY file
NEWS 9	Sep 16	CA Section Thesaurus available in CAPLUS and CA
NEWS 10	Oct 01	CASREACT Enriched with Reactions from 1907 to 1985
NEWS 11	Oct 24	BEILSTEIN adds new search fields
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NEWS 14	Nov 25	More calculated properties added to REGISTRY
NEWS 15	Dec 04	CSA files on STN
NEWS 16	Dec 17	PCTFULL now covers WP/PCT Applications from 1978 to date
NEWS 17	Dec 17	TOXCENTER enhanced with additional content
NEWS 18	Dec 17	Adis Clinical Trials Insight now available on STN
NEWS 19	Jan 29	Simultaneous left and right truncation added to COMPENDEX, ENERGY, INSPEC
NEWS 20	Feb 13	CANCERLIT is no longer being updated
NEWS 21	Feb 24	METADEX enhancements
NEWS 22	Feb 24	PCTGEN now available on STN
NEWS 23	Feb 24	TEMA now available on STN
NEWS 24	Feb 26	NTIS now allows simultaneous left and right truncation
NEWS 25	Feb 26	PCTFULL now contains images
NEWS 26	Mar 04	SDI PACKAGE for monthly delivery of multifile SDI results
NEWS 27	Mar 20	EVENTLINE will be removed from STN
NEWS 28	Mar 24	PATDPAFULL now available on STN
NEWS 29	Mar 24	Additional information for trade-named substances without structures available in REGISTRY
NEWS 30	Apr 11	Display formats in DGENE enhanced
NEWS 31	Apr 14	MEDLINE Reload
NEWS 32	Apr 17	Polymer searching in REGISTRY enhanced
NEWS 33	Jun 13	Indexing from 1947 to 1956 added to records in CA/CAPLUS
NEWS 34	Apr 21	New current-awareness alert (SDI) frequency in WPIDS/WPINDEX/WPIX
NEWS 35	Apr 28	RDISCLOSURE now available on STN
NEWS 36	May 05	Pharmacokinetic information and systematic chemical names added to PHAR
NEWS 37	May 15	MEDLINE file segment of TOXCENTER reloaded
NEWS 38	May 15	Supporter information for ENCOMPPAT and ENCOMPLIT updated
NEWS 39	May 16	CHEMREACT will be removed from STN
NEWS 40	May 19	Simultaneous left and right truncation added to WSCA
NEWS 41	May 19	RAPRA enhanced with new search field, simultaneous left and right truncation
NEWS 42	Jun 06	Simultaneous left and right truncation added to CBNB
NEWS 43	Jun 06	PASCAL enhanced with additional data
NEWS 44	Jun 20	2003 edition of the FSTA Thesaurus is now available

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```
 NEWS 45  Jun 25  HSDB has been reloaded

 NEWS EXPRESS  April 4 CURRENT WINDOWS VERSION IS V6.01a, CURRENT
               MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP),
               AND CURRENT DISCOVER FILE IS DATED 01 APRIL 2003
 NEWS HOURS    STN Operating Hours Plus Help Desk Availability
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 NEWS PHONE    Direct Dial and Telecommunication Network Access to STN
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FILE 'HOME' ENTERED AT 13:15:23 ON 01 JUL 2003

=> file reg
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     0.21       0.21

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STRUCTURE FILE UPDATES:   30 JUN 2003  HIGHEST RN 540462-79-1
DICTIONARY FILE UPDATES:  30 JUN 2003  HIGHEST RN 540462-79-1

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2003

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available.  See HELP
PROPERTIES for more information.  See STNote 27, Searching Properties
in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

=> s tetrahydrofolic
L1          43 TETRAHYDROFOLIC

=> s tetrahydrofolate
L2        1145 TETRAHYDROFOLATE

=> s l1 or l2
L3        1180 L1 OR L2

=> file caplus
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
```

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	ENTRY	SESSION
FULL ESTIMATED COST	8.84	9.05

FILE 'CAPLUS' ENTERED AT 13:16:24 ON 01 JUL 2003
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FILE COVERS 1907 - 1 Jul 2003 VOL 139 ISS 1
FILE LAST UPDATED: 30 Jun 2003 (20030630/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

```
=> s l3/prep
         10583 L3
       3021222 PREP/RL
L4         571 L3/PREP
                (L3 (L) PREP/RL)

=> s l4 and (sulphonic or sulfonic)
           815 SULPHONIC
         65738 SULFONIC
L5           2 L4 AND (SULPHONIC OR SULFONIC)

=> d l5 1- ibib abs hitstr
YOU HAVE REQUESTED DATA FROM 2 ANSWERS - CONTINUE? Y/(N):y

L5   ANSWER 1 OF 2  CAPLUS  COPYRIGHT 2003 ACS
ACCESSION NUMBER:        2001:148310  CAPLUS
DOCUMENT NUMBER:         134:326731
TITLE:                   Enantioselective catalyses. Part CXXXV.
                         Stereoselective hydrogenation of folic acid and
                         2-methylquinoxaline with optically active
                         rhodium(I)-phosphine complexes
AUTHOR(S):               Brunner, Henri; Rosenboem, Sabine
CORPORATE SOURCE:        Institut fur Anorganische Chemie, Universitat
                         Regensburg, D-93040, Germany
SOURCE:                  Monatshefte fuer Chemie (2000), 131(12), 1371-1382
                         CODEN: MOCMB7; ISSN: 0026-9247
PUBLISHER:               Springer-Verlag Wien
DOCUMENT TYPE:           Journal
LANGUAGE:                German
OTHER SOURCE(S):         CASREACT 134:326731
```

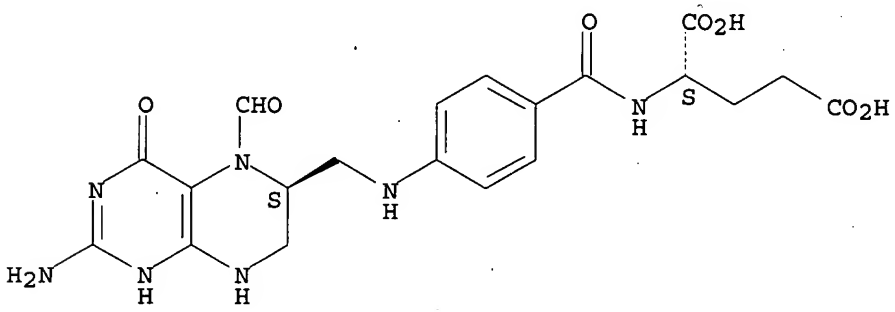
AB In the hydrogenation of the C:N double bonds of the pyrazine ring of folic acid to 5,6,7,8-tetrahydrofolic acid a new asym. center is formed at C(6) of the pteridine system. With Rh(I) catalysts made from optically active phosphines, which are immobilized on silica gel, the hydrogenation in aq. soln. can be controlled stereoselectively. The highest diastereomeric excess of .apprx.40% is obtained with (-)-BPPM-contg. catalysts. The hydrogenation of folic acid in aq. soln. is also possible homogeneously

with Rh(I)-phosphine catalysts, the ligands of which contain **sulfonic** acid groups and polyether fragments. The homogeneous hydrogenations proceed slower and with somewhat reduced diastereoselectivities compared to heterogeneous catalysis. The hydrogenation of 2-methylquinoxaline is a model system for the redn. of folic acid. Usual Rh(I)-phosphine catalysts afford only low enantioselectivities.

IT **68538-85-2P**, (6S)-5-Formyl-5,6,7,8-tetrahydrofolic acid
73951-54-9P, (6R)-5-Formyl-5,6,7,8-tetrahydrofolic acid
RL: PEP (Physical, engineering or chemical process); PUR (Purification or recovery); SPN (Synthetic preparation); **PREP (Preparation)**; PROC (Process)
(asym. hydrogenation of folic acid and methylquinoxaline catalyzed by rhodium phosphine complexes)

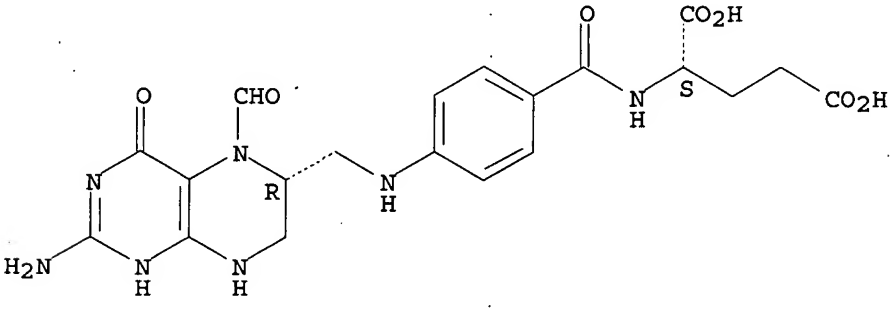
RN 68538-85-2 CAPLUS
CN L-Glutamic acid, N-[4-[[[(6S)-2-amino-5-formyl-1,4,5,6,7,8-hexahydro-4-oxo-6-pteridinyl]methyl]amino]benzoyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 73951-54-9 CAPLUS
CN L-Glutamic acid, N-[4-[[[(6R)-2-amino-5-formyl-1,4,5,6,7,8-hexahydro-4-oxo-6-pteridinyl]methyl]amino]benzoyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1992:612959 CAPLUS
DOCUMENT NUMBER: 117:212959
TITLE: Process for the preparation of (6S)- and (6R)-tetrahydrofolic acid
INVENTOR(S): Mueller, Hans Rudolf; Ulmann, Martin; Conti, Josef; Muerdel, Guenter
PATENT ASSIGNEE(S): EPROVA A.-G., Switz.

10/ 030,693

SOURCE: Eur. Pat. Appl., 8 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 495204	A1	19920722	EP 1991-121326	19911212
EP 495204	B1	19950614		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
CH 681303	A	19930226	CH 1991-108	19910116
RU 2099340	C1	19971220	RU 1991-5010253	19911206
ES 2075315	T3	19951001	ES 1991-121326	19911212
IL 100478	A1	19990312	IL 1991-100478	19911223
CA 2059103	AA	19920717	CA 1992-2059103	19920109
CA 2059103	C	19961217		
JP 04312586	A2	19921104	JP 1992-5095	19920114
JP 07039417	B4	19950501		
NO 9200197	A	19920717	NO 1992-197	19920115
FI 9200180	A	19920717	FI 1992-180	19920115
AU 9210254	A1	19920723	AU 1992-10254	19920115
AU 654993	B2	19941201		
CN 1063285	A	19920805	CN 1992-100247	19920115
CN 1030079	B	19951018		
HU 60272	A2	19920828	HU 1992-134	19920115
HU 207083	B	19930301		
ZA 9200291	A	19920930	ZA 1992-291	19920115
LV 10083	B	19950420	LV 1993-220	19930402
US 5324836	A	19940628	US 1993-44886	19930408

PRIORITY APPLN. INFO.: CH 1991-108 19910116
US 1992-821151 19920116

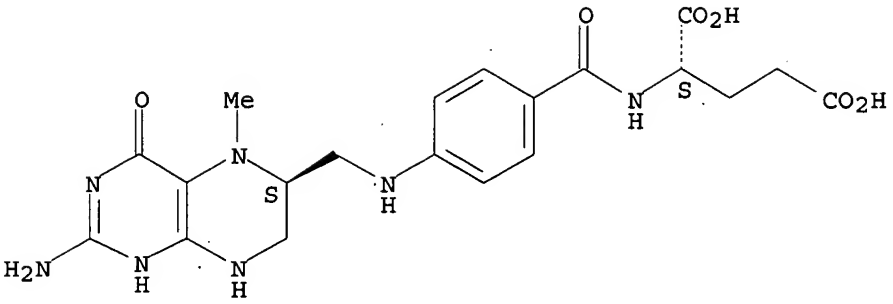
AB (6S)- (I) and (6R)-tetrahydrofolic acids and their salts with **sulfonic** acids or H2SO4 were prepd. by treatment of (6RS)-tetrahydrofolic acid (II) with **sulfonic** acids or H2SO4 followed by fractional crystn. of the addn. salts and optional treatment with base. Thus, 25.0 g II was added over 5 min to 14.3 g 4-MeC6H4SO3H (III) in 440 mL H2O contg. 0.1% HSCH2CH2OH at 60.degree.; the mixt. was kept 2-5 h at 40.degree. to give 16.9 g I.III of 86.7% diastereomeric purity; and recrystn. from 110 mL DMF and 220 mL H2O gave I.III of 97.5% enantiomeric purity.

IT **31690-09-2P 31690-11-6P 71963-69-4P**
80433-71-2P
RL: SPN (Synthetic preparation); **PREP (Preparation)**
(prepn. of)

RN 31690-09-2 CAPLUS

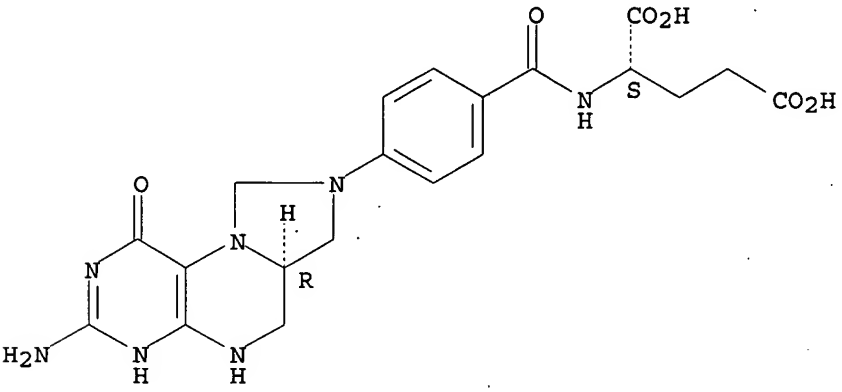
CN L-Glutamic acid, N-[4-[[[(6S)-2-amino-1,4,5,6,7,8-hexahydro-5-methyl-4-oxo-6-pteridinyl]methyl]amino]benzoyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



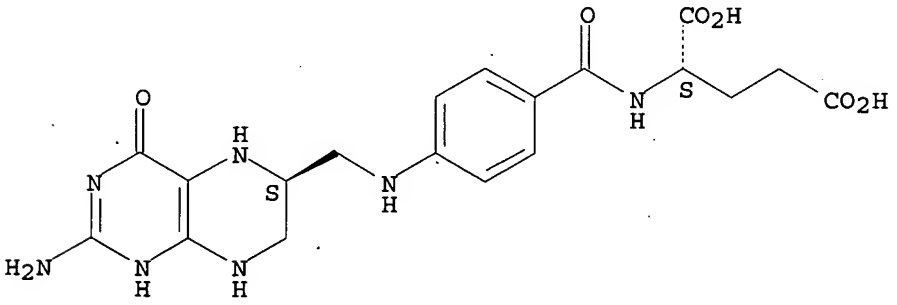
RN 31690-11-6 CAPLUS
CN L-Glutamic acid, N-[4-[(6aR)-3-amino-1,2,5,6,6a,7-hexahydro-1-oxoimidazo[1,5-f]pteridin-8(9H)-yl]benzoyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 71963-69-4 CAPLUS
CN L-Glutamic acid, N-[4-[[[(6S)-2-amino-1,4,5,6,7,8-hexahydro-4-oxo-6-pteridinyl]methyl]amino]benzoyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 80433-71-2 CAPLUS
CN L-Glutamic acid, N-[4-[[[(6S)-2-amino-5-formyl-1,4,5,6,7,8-hexahydro-4-oxo-6-pteridinyl]methyl]amino]benzoyl]-, calcium salt (1:1) (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

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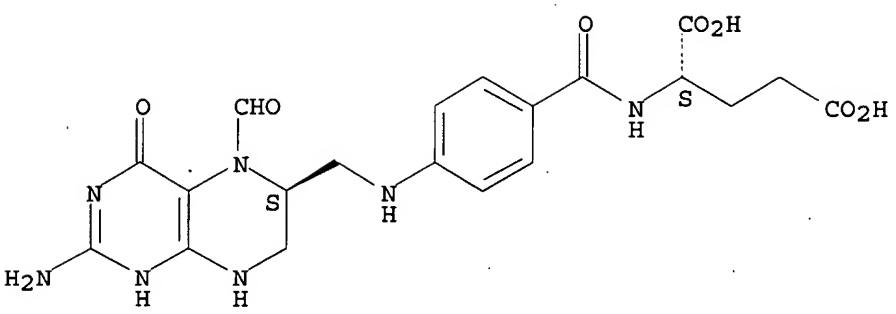

● Ca

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=> d his

     (FILE 'HOME' ENTERED AT 13:15:23 ON 01 JUL 2003)

     FILE 'REGISTRY' ENTERED AT 13:15:31 ON 01 JUL 2003
L1            43 S TETRAHYDROFOLIC
L2          1145 S TETRAHYDROFOLATE
L3          1180 S L1 OR L2

     FILE 'CAPLUS' ENTERED AT 13:16:24 ON 01 JUL 2003
L4           571 S L3/PREP
L5             2 S L4 AND (SULPHONIC OR SULFONIC)

=> s l4 and acid?
       4308366 ACID?
L6           344 L4 AND ACID?

=> s l6 not l5
L7           342 L6 NOT L5

=> s l7 and (separat? or diastereomer?)
        287313 SEPARAT?
         20149 DIASTEREOMER?
L8            30 L7 AND (SEPARAT? OR DIASTEREOMER?)

=> d l8 1- ibib abs hitstr
YOU HAVE REQUESTED DATA FROM 30 ANSWERS - CONTINUE? Y/(N):y

L8   ANSWER 1 OF 30  CAPLUS  COPYRIGHT 2003 ACS
ACCESSION NUMBER:         2000:155286  CAPLUS
DOCUMENT NUMBER:          133:40009
TITLE:                    Role of the Carbohydrate Moieties in Chiral
                          Recognition on Teicoplanin-Based LC Stationary Phases
AUTHOR(S):                Berthod, Alain; Chen, Xianghong; Kullman, John P.;
                          Armstrong, Daniel W.; Gasparrini, Francesco;
                          D'Acquarica, Ilaria; Villani, Claudio; Carotti, Angelo
CORPORATE SOURCE:         Department of Chemistry, University of Missouri-Rolla,
                          Rolla, MO, 65409, USA
SOURCE:                   Analytical Chemistry (2000), 72(8), 1767-1780
                          CODEN: ANCHAM; ISSN: 0003-2700
PUBLISHER:                American Chemical Society
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
```

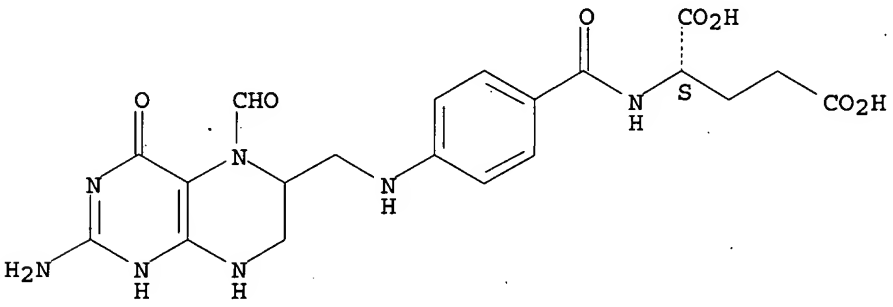
AB For this study, we used the macrocyclic antibiotic teicoplanin, a mol. consisting of an aglycon peptide "basket" with three attached carbohydrate (sugar) moieties. The sugar units were removed and the aglycon was purified. Two chiral stationary phases (CSPs) were prepd. in a similar way, one with the native teicoplanin mol. and the other with the aglycon. Twenty-six compds. were evaluated on the two CSPs with seven RPLC mobile phases and two polar org. mobile phases. The compds. were 13 amino **acids** or structurally related compds. (including DOPA, folinic **acid**, etc.) and 13 other compds. (such as carnitine, bromacil, etc.). The chromatog. results are given as the retention, selectivity, and resoln. factors along with the peak efficiency and the enantioselective free energy difference corresponding to the sepn. of the two enantiomers. The polarities of the two CSPs are similar. It is clearly established that the aglycon is responsible for the enantiosepn. of amino **acids**. The difference in enantioselective free energy between the aglycon CSP and the teicoplanin CSP was between 0.3 and 1 kcal/mol for amino **acid** enantiosepns. This produced resoln. factors 2-5 times higher with the aglycon CSP. Four non-amino **acid** compds. were sepd. only on the teicoplanin CSP. Six and five compds. were better sepd. on the teicoplanin and aglycon CSPs, resp. Although the sugar units decrease the resoln. of .alpha.-amino **acid** enantiomers, they can contribute significantly to the resoln. of a no. of non-amino **acid** enantiomeric pairs.

IT **58-05-9P**
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); PUR (Purification or recovery); BIOL (Biological study); **PREP (Preparation)**; PROC (Process)
(role of carbohydrate moieties in chiral recognition on teicoplanin-based LC stationary phases)

RN 58-05-9 CAPLUS

CN L-Glutamic acid, N-[4-[[(2-amino-5-formyl-1,4,5,6,7,8-hexahydro-4-oxo-6-pteridinyl)methyl]amino]benzoyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 2 OF 30 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1999:508420 CAPLUS

DOCUMENT NUMBER: 131:272150

TITLE: Synthesis of the .gamma.-sulfinic **acid** and .gamma.-nitro analogs of 5-deazatetrahydrofolic **acid**

AUTHOR(S): Forsch, Ronald A.; Wright, Joel E.; Rosowsky, Andre

CORPORATE SOURCE: Dana-Farber Cancer Institute and Department of Biological Chemistry and Molecular Pharmacology, Harvard Medical School, Boston, MA, 02115, USA

SOURCE: Heterocycles (1999), 51(8), 1789-1805
CODEN: HTCYAM; ISSN: 0385-5414

10/ 030,693

PUBLISHER: Japan Institute of Heterocyclic Chemistry
DOCUMENT TYPE: Journal
LANGUAGE: English

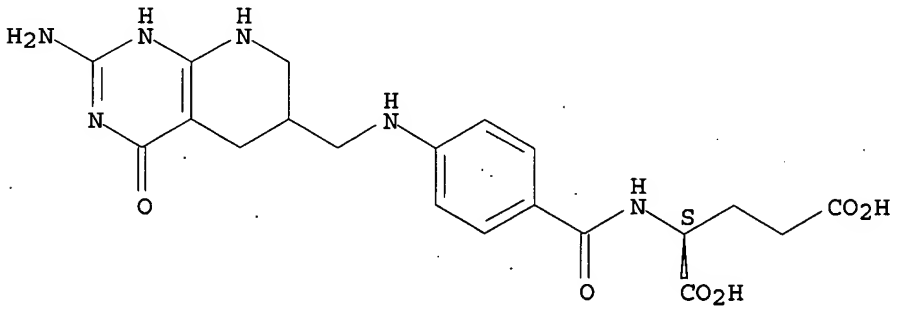
AB Analogs of 5-deaza-5,6,7,8-tetrahydrofolic **acid** with a .gamma.-sulfinic **acid** group or .gamma.-nitro group in place of the .gamma.-carboxyl group of the glutamate side chain were synthesized as **diastereomeric** mixts., and were tested for their ability to inhibit the growth of CCRF-CEM human leukemia cells in culture. The concn. of the .gamma.-sulfinic **acid** analog (7) giving 50% inhibition of growth during 120 h of continuous drug treatment was 21 .mu.M vs. 93 .mu.M for the .gamma.-nitro analog. The Ki of 7 as a competitive inhibitor of the influx of [3H]methotrexate into CCRF-CEM cells via the reduced folate carrier (RFC) was 5.0 .mu.M, a value close to the Km values typically cited in the literature for MTX and natural reduced folates. Thus, apart from any other mechanistic targets this compd. might have, 7 has the potential to deplete endogenous pools of reduced folates in dividing cells by interfering with RFC function.

IT **115499-24-6DP**, 5-Deazatetrahydrofolic **acid**, analogs
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); **PREP (Preparation)**
(synthesis of .gamma.-sulfinic **acid** and .gamma.-nitro analogs of 5-deazatetrahydrofolic **acid**)

RN 115499-24-6 CAPLUS

CN L-Glutamic acid, N-[4-[[(2-amino-1,4,5,6,7,8-hexahydro-4-oxopyrido[2,3-d]pyrimidin-6-yl)methyl]amino]benzoyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 3 OF 30 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:208450 CAPLUS
DOCUMENT NUMBER: 128:267960
TITLE: Crosslinked protein crystals as universal **separation** media
INVENTOR(S): Margolin, Alexey L.; Vilenchik, Lev Z.
PATENT ASSIGNEE(S): Altus Biologics Inc., USA; Margolin, Alexey L.; Vilenchik, Lev Z.
SOURCE: PCT Int. Appl., 115 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9813119	A1	19980402	WO 1997-US17167	19970924

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

AU 9747381 A1 19980417 AU 1997-47381 19970924
PRIORITY APPLN. INFO.: US 1996-719114 19960924
WO 1997-US17167 19970924

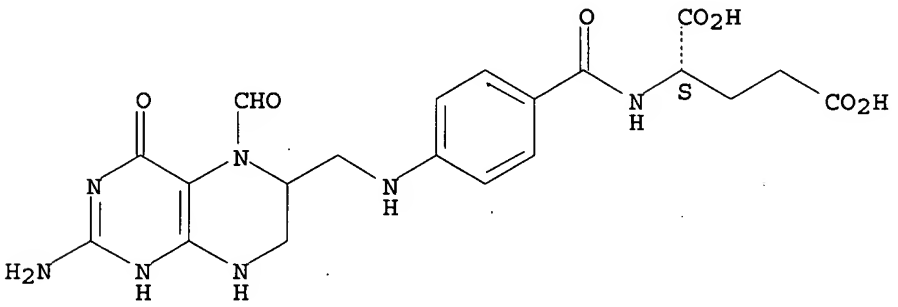
AB The present invention relates to the use of crosslinked protein crystals in methods, app. and systems for sepg. a substance or mol. of interest from a sample. According to a preferred embodiment of this invention, crosslinked protein crystals are used in chromatog. methods, app. and systems in which sepn. is based on a phys. or chem. property of that substance or mol. of interest. Advantageously, the crosslinked protein crystals which characterize the methods, app. and systems of this invention possess excellent mech. strength and well developed porous structure, demonstrate significant affinity and chiral selectivity and are extremely stable in aq. and org. solvents. These properties render the crystals particularly useful as sorbents for sepns., including size exclusion, affinity and chiral chromatog. Crosslinked bovine serum albumin crystals were prepd. and packed in a chromatog. column. Ketoprofen, suprofen, and naproxen were sepd. by affinity chromatog.

IT **58-05-9P**, Folinic **acid**
RL: ANT (Analyte); PUR (Purification or recovery); ANST (Analytical study); **PREP (Preparation)**
(crosslinked protein crystals as universal sepn. media)

RN 58-05-9 CAPLUS

CN L-Glutamic acid, N-[4-[[(2-amino-5-formyl-1,4,5,6,7,8-hexahydro-4-oxo-6-pteridinyl)methyl]amino]benzoyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 4 OF 30 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:105846 CAPLUS
DOCUMENT NUMBER: 128:141022
TITLE: Process for the preparation and **separation** of **diastereomeric** salts of folinic **acid**
INVENTOR(S): Felder, Ernst; Ripa, Giorgio; Distaso, Carlo
PATENT ASSIGNEE(S): Dibra S.p.A., Italy
SOURCE: U.S., 8 pp., Cont.-in-part of U.S. 5,599,931.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English

10/ 030,693

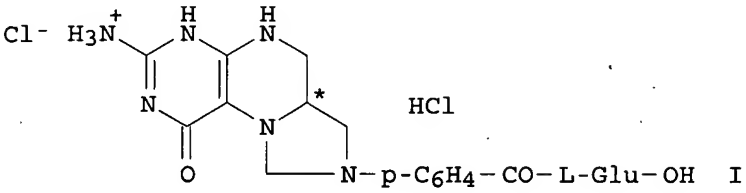
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5710271	A	19980120	US 1995-480097	19950607
US 5599931	A	19970204	US 1995-456767	19950601

PRIORITY APPLN. INFO.:

IT 1994-MI1193 A 19940608
US 1995-456767 A2 19950601
IT 1992-MI367 A 19920220
US 1994-290812 B1 19940817

GI



I

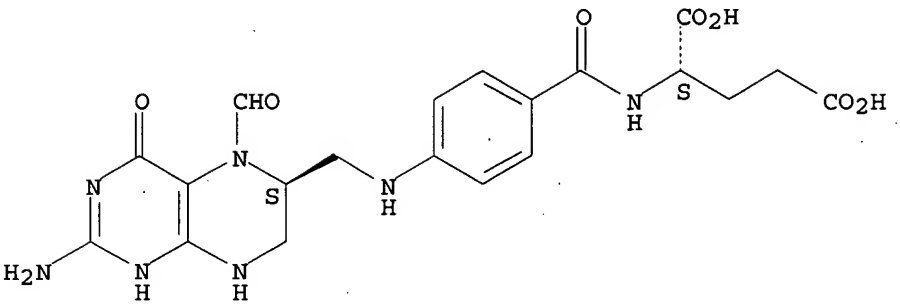
AB A process for the prepn. of the calcium salt of the essentially pure (6S) **diastereomer** of folinic **acid** is disclosed. The process includes hydrolyzing the racemic mixt. of (6RS)-5,10-methylene-5,6,7,8-tetrahydrofolic **acid** chloride hydrochloride (I; racemic center is *'d) with a diamine (such as ethylenediamine, 1,2-diaminopropane, 1,3-diaminopropane, 1,3-diamino-2-hydroxypropane, cis- or trans-1,2-diaminocyclohexane, piperazine, 2-methylpiperazine, 2,5-dimethylpiperazine, 1,4-dimethylpiperazine) in a reaction medium which is water or water/aprotic dipolar solvent (such as DMF, DMSO, dimethylacetamide, N-methylpyrrolidone, and hexamethylphosphoramide) to give the said diamine salts of (RS)-folinate in a molar ratio of 1:1. Subsequently, the more insol. salt of (R)- and (S)-folinate is crystd. by cooling the above reaction mixt. by adding an amt. of said aprotic dipolar solvent up to a max. water/aprotic dipolar solvent ratio of 1:60 by wt, followed by salification with aq. CaCl2 soln. at a pH range of 6.5-7.5. The remaining isomer in the mother liquors is crystd. and isolated in a similar work-up fashion.

IT **80433-71-2P 115940-48-2P**
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); **PREP (Preparation)**
(prepn. and sepn. of **diastereomeric** salts of folinic **acid**)

RN 80433-71-2 CAPLUS

CN L-Glutamic acid, N-[4-[[[(6S)-2-amino-5-formyl-1,4,5,6,7,8-hexahydro-4-oxo-6-pteridinyl]methyl]amino]benzoyl]-, calcium salt (1:1) (9CI) (CA INDEX NAME)

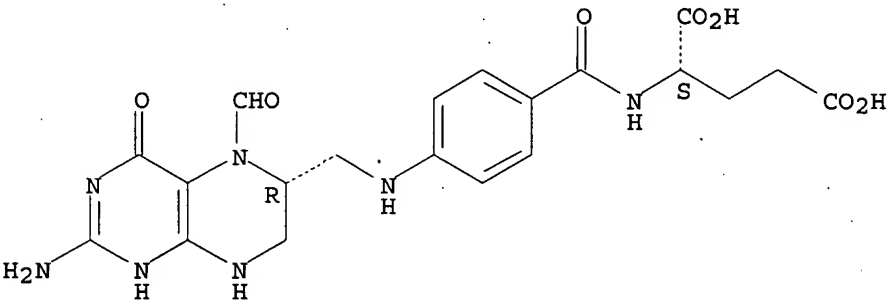
Absolute stereochemistry. Rotation (-).



● Ca

RN 115940-48-2 CAPLUS
CN L-Glutamic acid, N-[4-[[[(6R)-2-amino-5-formyl-1,4,5,6,7,8-hexahydro-4-oxo-6-pteridinyl]methyl]amino]benzoyl]-, calcium salt (1:1) (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



● Ca

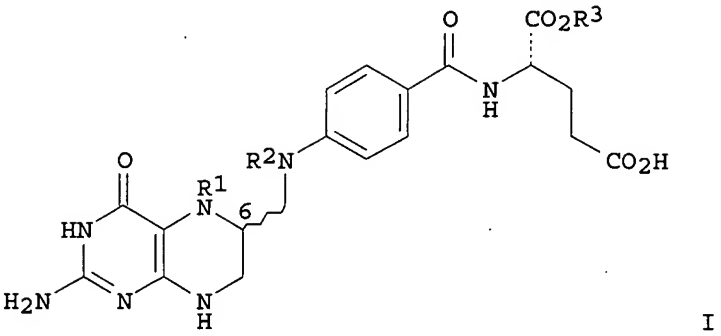
REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 5 OF 30 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:1341 CAPLUS
DOCUMENT NUMBER: 128:75672
TITLE: Process of **separating** the **diastereomers** of (6R,6S)-5,6,7,8-tetrahydrofolic **acid** derivatives
INVENTOR(S): Fitzhugh, Anthony L.; Akee, Rhone K.
PATENT ASSIGNEE(S): United States Dept. of Health and Human Services, USA
SOURCE: U.S., 7 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5698693	A	19971216	US 1992-977008	19921116

10/ 030,693

PRIORITY APPLN. INFO.: US 1992-977008 19921116
OTHER SOURCE(S): CASREACT 128:75672; MARPAT 128:75672
GI



I

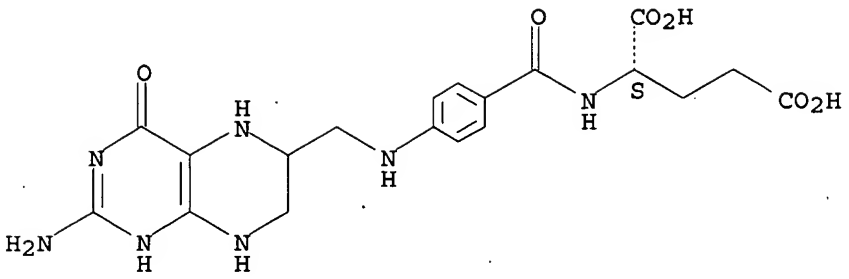
AB A method for resolving 5,6,7,8-tetrahydrofolic **acid** derivs. I (R1 = C1-6 alkyl, C1-6 alkylcarbonyl, C1-6 alkoxycarbonyl, CHO, wherein said alkyl, alkylcarbonyl, and alkoxycarbonyl may be substituted with halo, C1-6 alkoxy, Ph; R2 = H, C1-6 alkyl, C1-6 alkylcarbonyl, C1-6 alkoxycarbonyl, CHO, wherein said alkyl, alkylcarbonyl, and alkoxycarbonyl may be substituted with halo, C1-6 alkoxy, Ph; R1R2 = 1-carbon bridge; R3 = H) into **diastereomerically** pure 6R and 6S forms is described. The method comprises (1) .alpha.-esterification of the tetrahydrofolic **acid** deriv. to give .alpha.-monoesters I (R3 = C1-8 alkyl, C5-6 cycloalkyl, substituted C5-6 cycloalkyl, C6-10 aryl (Ph and naphthyl), substituted C6-10 aryl, C6-10 aryl-C1-8 alkyl, substituted C6-10 aryl-C1-8 alkyl, CHPh2, substituted diphenylmethyl, trialkylsilyl); (2) resoln. of the .alpha.-monoesters into pure **diastereomers**; and (3) deprotecting the resolved .alpha.-monoester to thereby produce the pure **diastereomer** of the original 5,6,7,8 tetrahydrofolic **acid** deriv. The resoln. step can be carried out by any conventional means including chromatog. or fractional crystn. The method results in abs. **diastereomeric** purity even when an achiral stationary phase is used for the resoln. Thus, esterification of 500 mg (6R,6S)-5-formyl-5,6,7,8-tetrahydrofolic **acid** (I; R1 = CHO, R2 = R3 = H) with 317 mg 2,6-dichlorobenzyl bromide and 56 mg Na2CO3 in 20 mL DMSO for 15 h at room temp. gave 293 mg of pure .alpha.-monoester I (R1 = CHO, R2 = H, R3 = CH2C6H3Cl2-2,6) after flash chromatog. The .alpha.-monoester was sepd. by chromatog. on a 41.4 mm .times. 25 cm silica gel column (av. particle size about 0.008 mm) with 90:10:03 (vol./vol.) CHCl3-MeOH-AcOH at 81 mL/min to give 81 mg pure (6R)-monoester and 86 mg (6S)-monoester. Sapon. of the sepd. .alpha.-monoesters with aq. NaOH gave enantiomerically pure title compds. I (R1 = CHO, R2 = R3 = H).

IT **135-16-0DP**, 5,6,7,8-Tetrahydrofolic **acid**, derivs.
RL: IMF (Industrial manufacture); PUR (Purification or recovery); RCT (Reactant); SPN (Synthetic preparation); **PREP (Preparation)**; RACT (Reactant or reagent)
(process for sepg. tetrahydrofolic **acid diastereomer** derivs. via esterification and chromatog. sepn.)

RN 135-16-0 CAPLUS

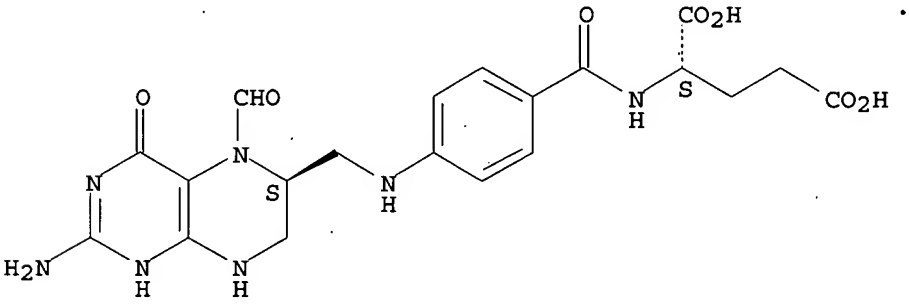
CN L-Glutamic acid, N-[4-[[(2-amino-1,4,5,6,7,8-hexahydro-4-oxo-6-pteridinyl)methyl]amino]benzoyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



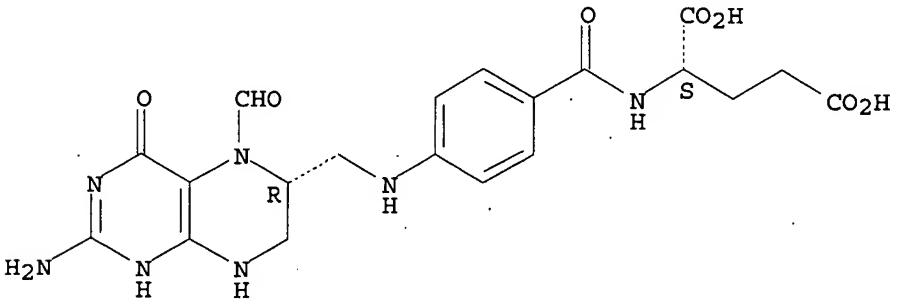
IT **68538-85-2P**, (6S)-5-Formyl-5,6,7,8-tetrahydrofolic **acid**
73951-54-9P
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); **PREP (Preparation)**; RACT (Reactant or reagent)
(process for sepg. tetrahydrofolic **acid diastereomer** derivs. via esterification and chromatog. sepn.)
RN 68538-85-2 CAPLUS
CN L-Glutamic acid, N-[4-[[[(6S)-2-amino-5-formyl-1,4,5,6,7,8-hexahydro-4-oxo-6-pteridinyl]methyl]amino]benzoyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 73951-54-9 CAPLUS
CN L-Glutamic acid, N-[4-[[[(6R)-2-amino-5-formyl-1,4,5,6,7,8-hexahydro-4-oxo-6-pteridinyl]methyl]amino]benzoyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L8 ANSWER 6 OF 30 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1997:98033 CAPLUS
DOCUMENT NUMBER: 126:212407
TITLE: Elucidation of vancomycin's enantioselective binding site using its copper complex

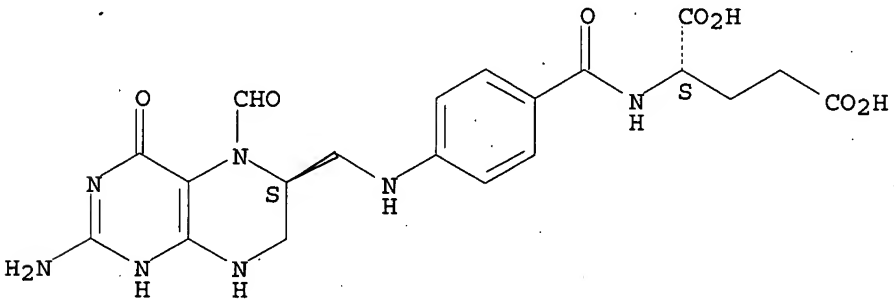
10/ 030,693

AUTHOR(S): Nair, Usha B.; Chang, Samuel S. C.; Armstrong, Daniel W.; Rawjee, Yasir Y.; Eggleston, Drake S.; McArdle, James V.
CORPORATE SOURCE: Dep. Chem., Univ. Missouri-Rolla, Rolla, MO, 65401, USA
SOURCE: Chirality (1996), 8(8), 590-595
CODEN: CHRLEP; ISSN: 0899-0042
PUBLISHER: Wiley-Liss
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Vancomycin forms a stable complex with Cu2+ in neutral aq. solns. The enantioselectivity of native vancomycin was compared to that of the copper-vancomycin complex using capillary electrophoresis. There were significant differences in their enantioselectivities. This can be attributed to the fact that copper ion coordinates with some of the same functional groups in vancomycin that are essential for chiral recognition and enantioresoln. An amine moiety that provides one of the more important enantioselective interactions was identified. This chiral interaction site was illustrated using a color-coded, space-filling model of the x-ray crystal structure of the copper-vancomycin complex. Successful enantioselective interactions at lower pHs were attributed to the partial dissocn. of the copper-vancomycin complex.

IT **68538-85-2P 73951-54-9P**
RL: PRP (Properties); PUR (Purification or recovery); **PREP (Preparation)**
(elucidation of vancomycin enantioselective binding site via its copper complex)

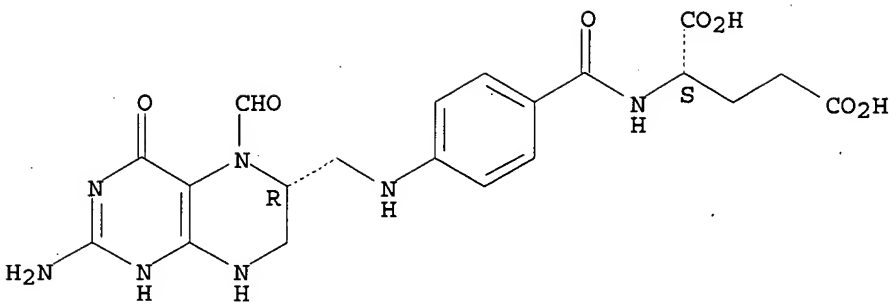
RN 68538-85-2 CAPLUS
CN L-Glutamic acid, N-[4-[[[(6S)-2-amino-5-formyl-1,4,5,6,7,8-hexahydro-4-oxo-6-pteridinyl]methyl]amino]benzoyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



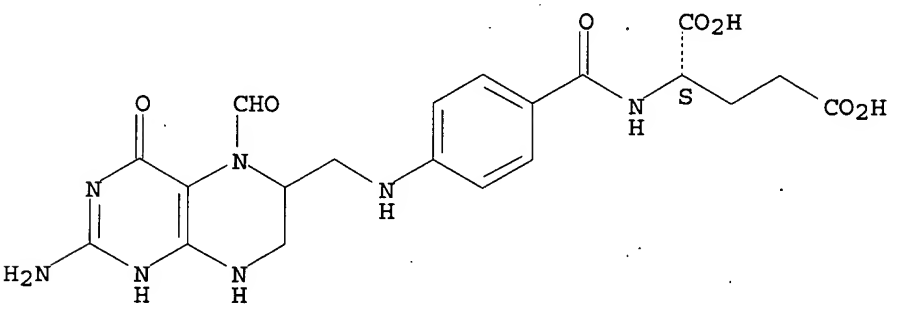
RN 73951-54-9 CAPLUS
CN L-Glutamic acid, N-[4-[[[(6R)-2-amino-5-formyl-1,4,5,6,7,8-hexahydro-4-oxo-6-pteridinyl]methyl]amino]benzoyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



IT **58-05-9P**, Leucovorin
RL: PUR (Purification or recovery); **PREP (Preparation)**
(elucidation of vancomycin enantioselective binding site via its copper complex)
RN 58-05-9 CAPLUS
CN L-Glutamic acid, N-[4-[[(2-amino-5-formyl-1,4,5,6,7,8-hexahydro-4-oxo-6-pteridinyl)methyl]amino]benzoyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L8 ANSWER 7 OF 30 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1997:53468 CAPLUS
DOCUMENT NUMBER: 126:171861
TITLE: Asymmetric catalysis. Part 105. Stereoselective hydrogenation of folic **acid** with immobilized optically active rhodium(I)/diphosphine catalysts
AUTHOR(S): Brunner, Henri; Bublak, Petra; Helget, Martina
CORPORATE SOURCE: Inst. Anorganische Chem., Univ. Regensburg, Regensburg, D-93053, Germany
SOURCE: Chemische Berichte/Recueil (1997), 130(1), 55-61
CODEN: CHBRFW
PUBLISHER: VCH
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 126:171861
AB For the hydrogenation of the C:N bonds in the pyrazine ring of folic **acid** optically active Rh(I)/diphosphine complexes immobilized on supports such as silica gel or Al2O3 were used. The redn. was carried out at 50 bar H-pressure in an aq. soln. buffered to pH 7. Thus, 5,6,7,8-tetrahydrofolic **acid** was obtained which contains a new sym. center at C(6) of the pterin system. Therefore, in combination with the (S) configuration of the natural L-glutamic **acid** part of the mol. 2 **diastereomers** with (6S,S) and (6R,S) configuration arise. The relatively unstable tetrahydrofolic **acid** was converted into folinic **acid** by treatment with HCO2Me/HCO2H in a 5:1 mixt. of

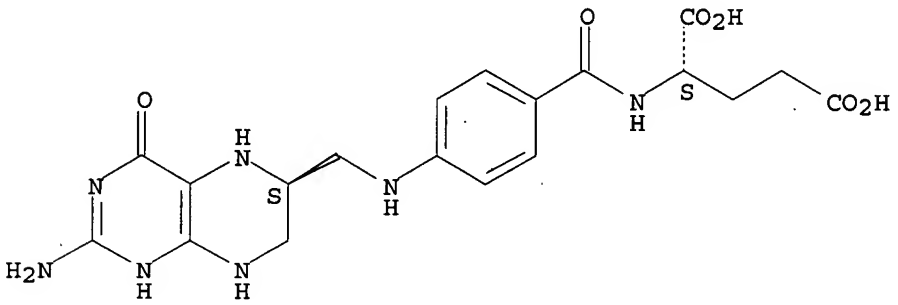
DMSO/pyridine. The **diastereomers** were sepd. by silica gel HPLC. To the column bovine serum albumin (BSA) is covalently bound. With optically active Rh(I)/diphosphine catalysts, immobilized on silica gel supports, a diastereoselectivity of .ltoreq.90% was achieved in the hydrogenation of folic **acid**.

IT **71963-69-4P**, (6S)-5,6,7,8-Tetrahydrofolic **acid**
RL: RCT (Reactant); SPN (Synthetic preparation); **PREP (Preparation)**; RACT (Reactant or reagent)
(stereoselective hydrogenation of folic **acid** with rhodium/diphosphine catalysts)

RN 71963-69-4 CAPLUS

CN L-Glutamic acid, N-[4-[[[(6S)-2-amino-1,4,5,6,7,8-hexahydro-4-oxo-6-pteridinyl]methyl]amino]benzoyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

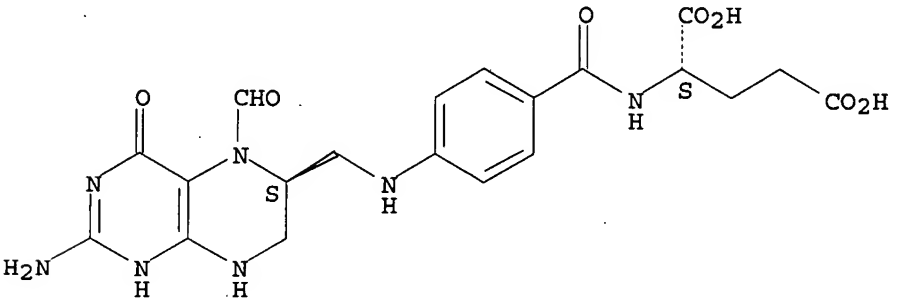


IT **68538-85-2P**, (6S)-Leucovorin **73951-54-9P**, (6R)-Leucovorin
RL: SPN (Synthetic preparation); **PREP (Preparation)**
(stereoselective hydrogenation of folic **acid** with rhodium/diphosphine catalysts)

RN 68538-85-2 CAPLUS

CN L-Glutamic acid, N-[4-[[[(6S)-2-amino-5-formyl-1,4,5,6,7,8-hexahydro-4-oxo-6-pteridinyl]methyl]amino]benzoyl]- (9CI) (CA INDEX NAME)

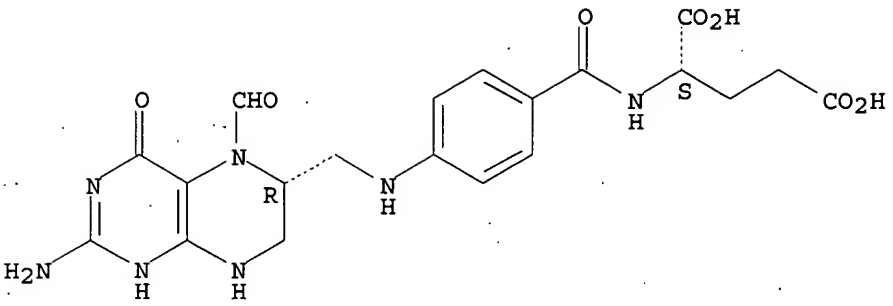
Absolute stereochemistry. Rotation (-).



RN 73951-54-9 CAPLUS

CN L-Glutamic acid, N-[4-[[[(6R)-2-amino-5-formyl-1,4,5,6,7,8-hexahydro-4-oxo-6-pteridinyl]methyl]amino]benzoyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



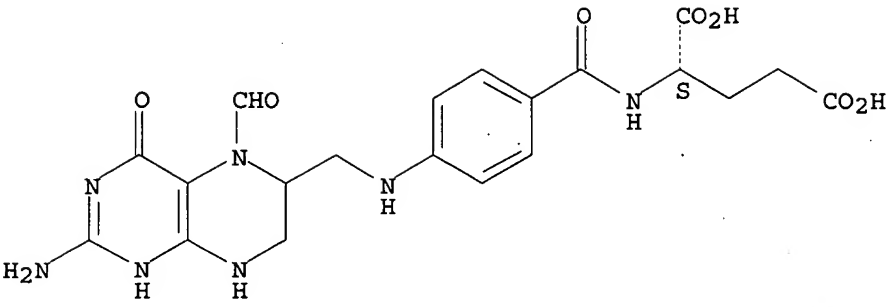
L8 ANSWER 8 OF 30 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1996:750105 CAPLUS
DOCUMENT NUMBER: 126:65263
TITLE: **Separation** of the **acids** in Ligustici Rhizoma by reversed electroosmotic flow capillary electrophoresis
AUTHOR(S): Weng, Wu-Che; Sheu, Shuenn-Jyi
CORPORATE SOURCE: Department Chemistry, National Taiwan Normal University, Taipei, Taiwan
SOURCE: Chinese Pharmaceutical Journal (Taipei) (1996), 48(3), 185-195
CODEN: CPHJEP
PUBLISHER: Pharmaceutical Society of Republic of China
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A facile method employing reversed electroosmotic flow capillary electrophoresis was developed for the sepn. of phthalic **acid**, protocatechuic **acid**, caffeic **acid**, folic **acid** , p-hydroxybenzoic **acid**, nicotinic **acid**, vanillic **acid**, ferulic **acid**, folinic **acid** and p-hydroxycinnamic **acid**. A buffer soln. consisting of 8 mM sodium borate, 3 mM sodium dihydrogen phosphate, 9 mM lauryltrimethylammonium chloride and acetontrile (7:3) was found to be most suitable for this sepn., whereby the contents of seven **acids** (1, 2, 3, 5, 6, 7 and 8) in a crude Ligustici rhizoma ext. could easily be detd. within 12 min. The effects of pH, EOF (electroosmotic flow) modifier concn. and org. modifier (acetonitrile) concn. on the migration behavior of the solutes were studied.

IT **58-05-9P**, Folinic **acid**
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); **PREP (Preparation)**; USES (Uses)
(sepn. of the **acids** in Ligustici Rhizoma by reversed electroosmotic flow capillary electrophoresis)

RN 58-05-9 CAPLUS
CN L-Glutamic acid, N-[4-[[(2-amino-5-formyl-1,4,5,6,7,8-hexahydro-4-oxo-6-pteridinyl)methyl]amino]benzoyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L8 ANSWER 9 OF 30 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1996:181575 CAPLUS
DOCUMENT NUMBER: 124:233144
TITLE: Preparation and **separation** of **diastereomeric** salts of folinic **acid**
INVENTOR(S): Felder, Ernst; Ripa, Giorgio; Distaso, Carlo
PATENT ASSIGNEE(S): Bracco S.p.A., Italy; Dibra S.p.A.
SOURCE: PCT Int. Appl., 24 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9533749	A1	19951214	WO 1995-EP2073	19950531
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MX, NO, NZ, PL, PT, RO, RU, SE, SG, SI, SK, TJ, TM, TT, UA, US, UZ				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9526726	A1	19960104	AU 1995-26726	19950531
EP 755397	A1	19970129	EP 1995-921797	19950531
EP 755397	B1	19980819		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, NL, PT, SE				
JP 10500972	T2	19980127	JP 1995-500330	19950531
AT 169918	E	19980915	AT 1995-921797	19950531
ZA 9504692	A	19960129	ZA 1995-4692	19950607
IN 181757	A	19980912	IN 1995-MA686	19950607

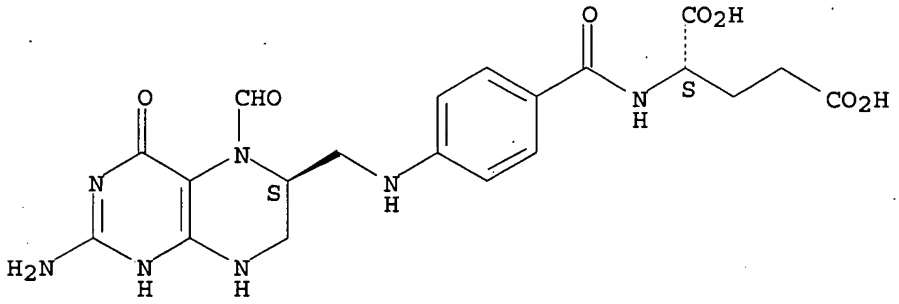
PRIORITY APPLN. INFO.: IT 1994-MI1193 A 19940608
WO 1995-EP2073 W 19950531

AB The (6S) and (6R) **diastereomers** of folinic **acid** salts with .gtoreq.dibasic amines are prepd. via hydrolysis of (6RS)-5,10-methylene-5,6,7,8-tetrahydrofolic **acid** chloride hydrochloride (I) with a .gtoreq.dibasic amine, subsequent sepn. of the **diastereomeric** salts, and optional conversion to Ca salts. Thus, I in dimethylacetamide/H2O was heated 5 h with piperazine; the soln. was dild. with dimethylacetamide and cooled to 15.degree. to ppt. piperazine (6S)-folinate over 48 h. The product had an optical purity >98%.

IT **80433-71-2P 115940-48-2P**
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); **PREP (Preparation)**
(prepn. and sepn. of **diastereomeric** salts of folinic **acid**)

RN 80433-71-2 CAPLUS
CN L-Glutamic acid, N-[4-[[[(6S)-2-amino-5-formyl-1,4,5,6,7,8-hexahydro-4-oxo-6-pteridinyl]methyl]amino]benzoyl]-, calcium salt (1:1) (9CI) (CA INDEX NAME)

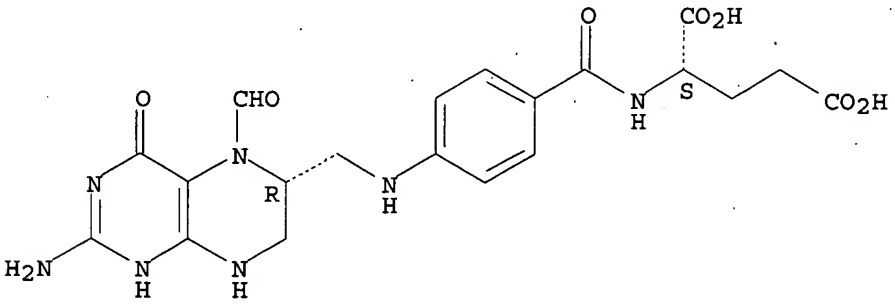
Absolute stereochemistry. Rotation (-).



● Ca

RN 115940-48-2 CAPLUS
CN L-Glutamic acid, N-[4-[[[(6R)-2-amino-5-formyl-1,4,5,6,7,8-hexahydro-4-oxo-6-pteridinyl]methyl]amino]benzoyl]-, calcium salt (1:1) (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



● Ca

L8 ANSWER 10 OF 30 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1995:986333 CAPLUS
DOCUMENT NUMBER: 124:28995
TITLE: Macrocyclic antibiotics as **separation** agents
INVENTOR(S): Armstrong, Daniel
PATENT ASSIGNEE(S): University of Missouri, USA
SOURCE: PCT Int. Appl., 71 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 9522390	A1	19950824	WO 1995-US2071	19950217
W: JP, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 748247	A1	19961218	EP 1995-911045	19950217
R: CH, DE, FR, GB, IT, LI				
JP 10501727	T2	19980217	JP 1995-521947	19950217
US 5626757	A	19970506	US 1995-532581	19950929
US 5874005	A	19990223	US 1997-851485	19970505
US 5964996	A	19991012	US 1998-187369	19981106

PRIORITY APPLN. INFO.:
US 1994-198409 19940222
WO 1995-US2071 19950217
US 1995-532581 19950929
US 1997-851485 19970505

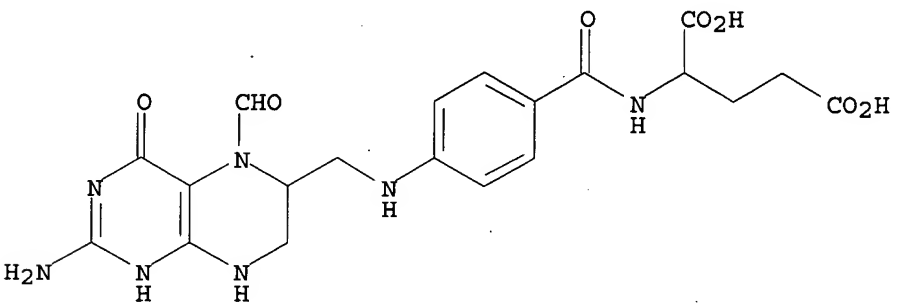
AB Macrocyclic antibiotics having ring structures with at least 10 members act as sepn. agents in crystn., pptn., filtration, electrophoresis and chromatog. The macrocyclic antibiotics include ansamacrolides, macrolides, macrocyclic peptides, polyenes and their derivs. The process has been found to be esp. advantageous for sepn. of optical isomers by electrophoresis and chromatog. Thus, vancomycin was treated with CN(CH2)3Si(OEt)3 and bonded to silica gel. The gel-bound vancomycin was used as a stationary phase to resolve coumachlor by reversed-phase chromatog.

IT **22350-60-3P**
RL: PUR (Purification or recovery); **PREP (Preparation)**
(macrocyclic antibiotics as chiral agents in chromatog. and electrophoretic sepns.)

RN 22350-60-3 CAPLUS

CN Glutamic acid, N-[4-[[(2-amino-5-formyl-1,4,5,6,7,8-hexahydro-4-oxo-6-pteridinyl)methyl]amino]benzoyl]- (9CI) (CA INDEX NAME)

Currently available stereo shown.



L8 ANSWER 11 OF 30 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1995:356904 CAPLUS
DOCUMENT NUMBER: 122:109342
TITLE: Method for the industrial preparation of (6S) folic **acid** derivatives by chromatographic **separation**
INVENTOR(S): Ambrosini, Leonardo; Sala, Bruno
PATENT ASSIGNEE(S): Irca S.p.A. - Industrie Ricerche Chimiche d'Albano, Italy
SOURCE: Eur. Pat. Appl., 6 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

10/ 030,693

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 627435	A1	19941207	EP 1993-108752	19930601
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
CA 2097884	AA	19941207	CA 1993-2097884	19930607
ZA 9304111	A	19940117	ZA 1993-4111	19930610
JP 06345765	A2	19941220	JP 1993-166252	19930610
IN 176058	A	19960106	IN 1993-CA331	19930615
CN 1096785	A	19941228	CN 1993-107281	19930619
CN 1039716	B	19980909		
BR 9302451	A	19950117	BR 1993-2451	19930623
AU 9341542	A1	19950119	AU 1993-41542	19930625
RU 2109015	C1	19980420	RU 1993-37415	19930716

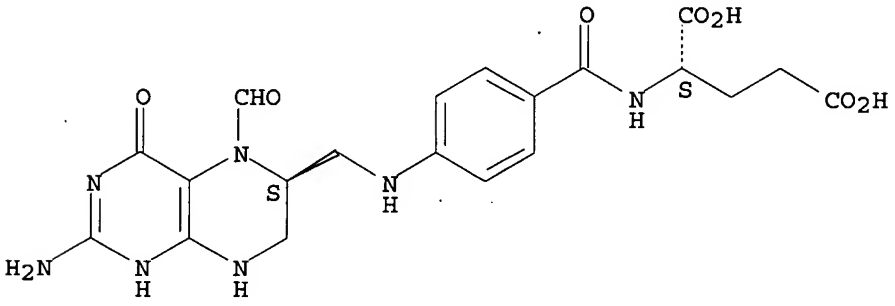
PRIORITY APPLN. INFO.: EP 1993-108752 19930601
OTHER SOURCE(S): MARPAT 122:109342

AB The method particularly suitable for the prepn. of 5-methyl-(6S)-tetrahydrofolic **acid** and 5-formyl-(6S)-tetrahydrofolic **acid**, comprises sepg. a soln. of the two (6RS) diastereoisomers on a chromatog. column wherein the sepg. agent is an albumin in a buffered soln. having pH .apprx.5.

IT **80433-71-2P**
RL: IMF (Industrial manufacture); **PREP (Preparation)**
(method for the industrial prepn. of (6S) folic **acid** derivs. by chromatog. sepn.)

RN 80433-71-2 CAPLUS
CN L-Glutamic acid, N-[4-[[[(6S)-2-amino-5-formyl-1,4,5,6,7,8-hexahydro-4-oxo-6-pteridinyl]methyl]amino]benzoyl]-, calcium salt (1:1) (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



O Ca

L8 ANSWER 12 OF 30 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1995:320833 CAPLUS
DOCUMENT NUMBER: 122:142711
TITLE: Highly enantioselective capillary electrophoretic **separations** with dilute solutions of the macrocyclic antibiotic ristocetin A
AUTHOR(S): Armstrong, Daniel W.; Gasper, Mary P.; Rundlett, Kimber L.
CORPORATE SOURCE: Department of Chemistry, University of Missouri-Rolla, Rolla, MO, 65401, USA
SOURCE: Journal of Chromatography, A (1995), 689(2), 285-304
CODEN: JCRAEY; ISSN: 0021-9673
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal

10/ 030,693

LANGUAGE: English

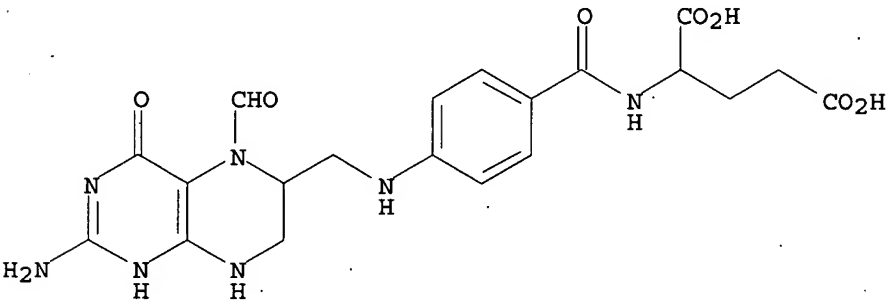
AB Ristocetin A is one of a series of structurally related amphoteric, glycopeptide, macrocyclic antibiotics. These compds. have several features that make them attractive as chiral selectors. These include spatially oriented functional groups that are known to provide the types of interactions that are conducive to enantio-recognition, a somewhat rigid "pocket" that can provide a site for hydrophobic interactions and polar, flexible arms (i.e., pendent sugar moieties) that can rotate to hydrogen bond and otherwise interact with a variety of chiral analytes. In addn., these compds. are sufficiently sol. in water, aq. buffers and aq.-org. solvents that are commonly used in capillary electrophoresis (CE). The use and optimization of ristocetin A as a chiral selector in CE is discussed. Over 120 racemates are resolved including a variety of N-blocked amino **acids**, non-steroidal anti-inflammatory compds. and a large no. of biol. important compds. contg. carboxylic **acid** groups (e.g., mandelic **acid** derivs., lactic **acid** derivs., folinic **acid**, tropic **acid**).

IT **22350-60-3P**
RL: PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(highly enantioselective capillary electrophoretic sepns. with dil. solns. of the macrocyclic antibiotic ristocetin A)

RN 22350-60-3 CAPLUS

CN Glutamic acid, N-[4-[[(2-amino-5-formyl-1,4,5,6,7,8-hexahydro-4-oxo-6-pteridinyl)methyl]amino]benzoyl]- (9CI) (CA INDEX NAME)

Currently available stereo shown.



L8 ANSWER 13 OF 30 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1994:435195 CAPLUS
DOCUMENT NUMBER: 121:35195
TITLE: Process for the preparation of (6S)-5,6,7,8-tetrahydrofolic **acid**.
INVENTOR(S): Jequier, Pascal; Marazza, Fabrizio
PATENT ASSIGNEE(S): Sapec s.a. Fine Chemicals, Switz.
SOURCE: Eur. Pat. Appl., 6 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 600460	A1	19940608	EP 1993-119354	19931201
EP 600460	B1	19990217		
R: CH, DE, ES, FR, GB, IT, LI				
CH 686672	A	19960531	CH 1992-3674	19921201
JP 06211857	A2	19940802	JP 1993-301646	19931201

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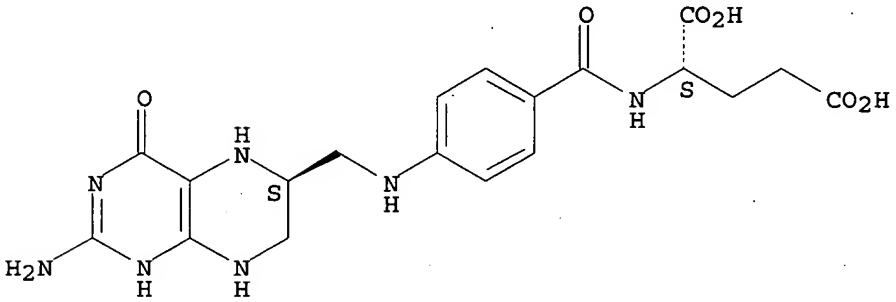
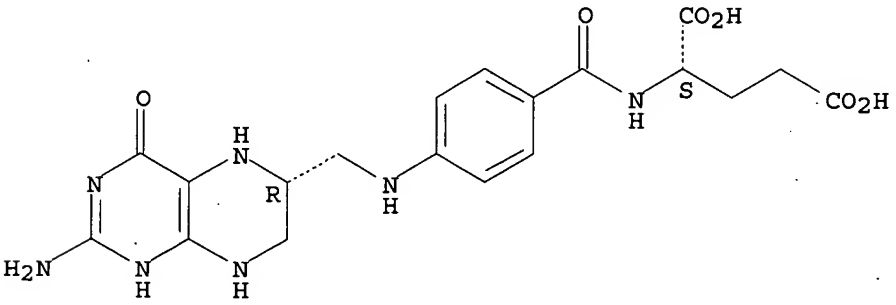
JP 2588363 B2 19970305
US 5489684 A 19960206 US 1993-159542 19931201
ES 2129486 T3 19990616 ES 1993-119354 19931201
PRIORITY APPLN. INFO.: CH 1992-3674 19921201
AB A process for the prepn. of >75% **diastereomerically** pure (6S)-5,6,7,8-tetrahydrofolic **acid** comprises the selective crystn. of racemic alkali tetrahydrofolate at pH 4.8-5.3. The use of (6S)-5,6,7,8-tetrahydrofolic **acid** the the synthesis of tetrahydrofolate derivs., such as L-folinic **acid** [(S)-Leucovorin], (6S)-5-Methyltetrahydrofolic **acid**, and L-(+)-Methylenetetrahydrofolic **acid** is claimed.
IT **71963-69-4P**, (6S)-Tetrahydrofolic **acid**
74708-38-6P, (6R)-Tetrahydrofolic **acid**
RL: SPN (Synthetic preparation); **PREP (Preparation)**
(prepn. of, via selective crystn. from racemate)
RN 71963-69-4 CAPLUS
CN L-Glutamic acid, N-[4-[[[(6S)-2-amino-1,4,5,6,7,8-hexahydro-4-oxo-6-pteridinyl]methyl]amino]benzoyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 74708-38-6 CAPLUS
CN L-Glutamic acid, N-[4-[[[(6R)-2-amino-1,4,5,6,7,8-hexahydro-4-oxo-6-pteridinyl]methyl]amino]benzoyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L8 ANSWER 14 OF 30 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1994:321389 CAPLUS
DOCUMENT NUMBER: 120:321389
TITLE: Efficient expression of E. coli dihydrofolate reductase gene by an in vitro translation system using phosphorothioate mRNA
AUTHOR(S): Tohda, Hideki; Chikazumi, Nobutoshi; Ueda, Takuya; Nishikawa, Kazuya; Watanabe, Kimitsuna
CORPORATE SOURCE: Department of Biological Sciences, Faculty of

10/ 030,693

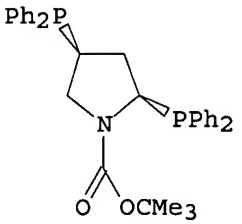
Bioscience and Biotechnology, Tokyo Institute of Technology, Nagatsuta, Midori-ku, Yokohama, 227, Japan
SOURCE: Journal of Biotechnology (1994), 34(1), 61-9
CODEN: JBITD4; ISSN: 0168-1656
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Dihydrofolate reductase (DHFR) of Escherichia coli was synthesized in a cell-free translation system of E. coli directed by phosphorothioate-contg. mRNA (thio-mRNA) which was polymd. by an in vitro transcription of the DHFR gene in the presence of SP **diastereomers** of ribonucleoside 5'-O-(1-thiotriphosphates). The mol. wts. of the products thus obtained were identical to those with the unsubstituted mRNA. The thio-mRNA for DHFR showed higher translational activities than the corresponding unsubstituted mRNA. This effectiveness may have resulted from the higher stability of thio-mRNA in the cell-free translation system. Among the various types of thio-mRNAs, the single substitution of adenosine residues was most effective in translational activity. This higher translational activity of thio-mRNA compared with the unsubstituted mRNA was also demonstrated in a continuous flow cell-free system. Therefore, introduction of S atoms into phosphodiester bonds of mRNA appears to be a useful strategy for the stabilization of mRNA in large-scale protein prodn. in vitro.
IT **9002-03-3P**, Dihydrofolate reductase
RL: BMF (Bioindustrial manufacture); BIOL (Biological study); **PREP (Preparation)**
(manuf. of, of Escherichia coli with in vitro translation system using phosphorothioate mRNA)
RN 9002-03-3 CAPLUS
CN Dehydrogenase, tetrahydrofolate (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L8 ANSWER 15 OF 30 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1994:107741 CAPLUS
DOCUMENT NUMBER: 120:107741
TITLE: Process for diastereoselective hydration of folic **acid** to tetrahydrofolic **acid**
INVENTOR(S): Brunner, Henri; Huber, Christian; Bublak, Petra
PATENT ASSIGNEE(S): BASF A.-G., Germany
SOURCE: Eur. Pat. Appl., 11 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 551642	A1	19930721	EP 1992-121772	19921222
R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, NL, SE				
DE 4200933	A1	19930722	DE 1992-4200933	19920116
CA 2086911	AA	19930717	CA 1993-2086911	19930107
JP 06009635	A2	19940118	JP 1993-4774	19930114
JP 08002902	B4	19960117		

PRIORITY APPLN. INFO.: DE 1992-4200933 19920116
GI



III

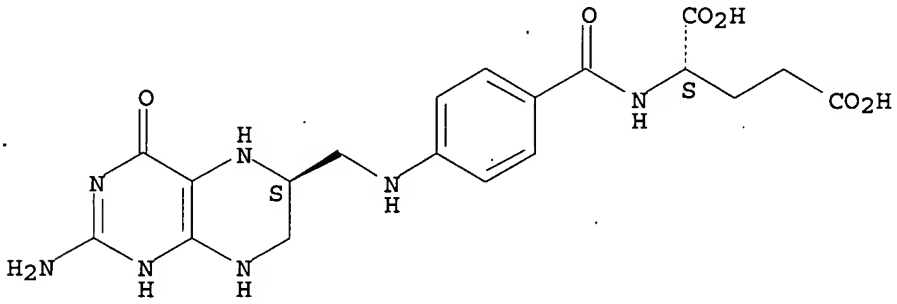
AB Folic **acid** (I) was diastereoselectively hydrogenated to tetrahydrofolic **acid** (II) in the presence of an immobilized Rh(I) complex with an optically active org. diphosphine in an aq. buffer at pH 3-12 at >20 bar H and >60.degree. Thus, [Rh(COD)Cl]2 and (-)-BPPM (III) were kept with silica gel in CH2Cl2 to give a yellow-orange catalyst powder, which was used to hydrogenate I in pH 7.0 phosphate buffer at 45 bar H and 80.degree. to give 100% hydrogenation and 49-51% **diastereomeric** excess for 6S, s-II.

IT **71963-69-4P**, (6S)-Tetrahydrofolic **acid**
74708-38-6P
RL: SPN (Synthetic preparation); **PREP (Preparation)**
(prepn. of, via diastereoselective hydrogenation of folic **acid** using immobilized rhodium(I) catalysts)

RN 71963-69-4 CAPLUS

CN L-Glutamic acid, N-[4-[[[(6S)-2-amino-1,4,5,6,7,8-hexahydro-4-oxo-6-pteridinyl]methyl]amino]benzoyl]- (9CI) (CA INDEX NAME)

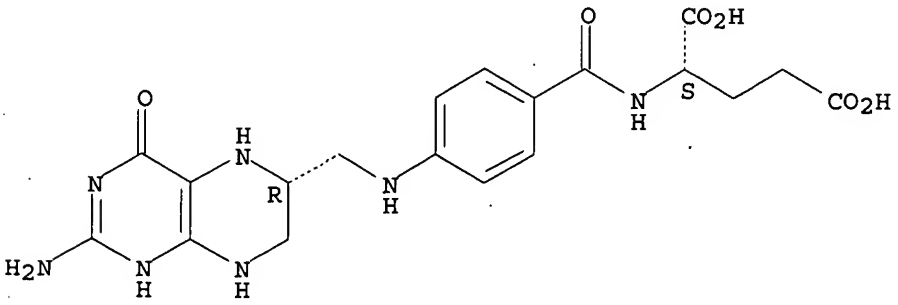
Absolute stereochemistry.



RN 74708-38-6 CAPLUS

CN L-Glutamic acid, N-[4-[[[(6R)-2-amino-1,4,5,6,7,8-hexahydro-4-oxo-6-pteridinyl]methyl]amino]benzoyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L8 ANSWER 16 OF 30 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1994:31226 CAPLUS
DOCUMENT NUMBER: 120:31226
TITLE: Process for **separating** stereoisomers of folinic **acid** via polyamine salts
INVENTOR(S): Ripa, Giorgio; Piva, Rodolfo; Felder, Ernst
PATENT ASSIGNEE(S): Bracco S.p.A., Italy
SOURCE: PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

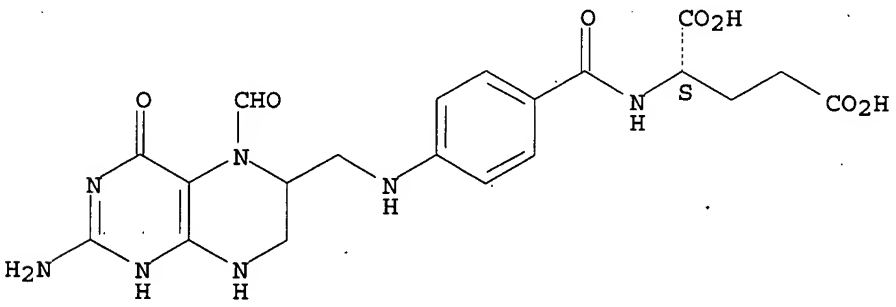
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9317022	A1	19930902	WO 1993-EP361	19930216
W: JP, KR, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 626965	A1	19941207	EP 1993-903973	19930216
EP 626965	B1	19980701		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, NL, PT, SE				
JP 07506813	T2	19950727	JP 1993-514507	19930216
JP 3162073	B2	20010425		
AT 167864	E	19980715	AT 1993-903973	19930216

PRIORITY APPLN. INFO.: IT 1992-MI367 A 19920220
WO 1993-EP361 W 19930216

AB The (6R)- and (6S)-**diastereomers** of folinic **acid** were sepd. by (1) salification with aliph. acyclic or cyclic di- or polyamines in solvents contg. .gtoreq.1 of dipolar aprotic solvents, H2O, or H2O-sol. protic org. solvents, (2) crystn., (3) purifn. by recrystn., and (4) isolation. Thus, (6RS)-folinic **acid** (I) in dimethylacetamide was treated with H2NCH2CH2NH2 (II) in dimethylacetamide at 5-35.degree. followed by stirring at 5-25.degree. to give I.II. This was recrystd. in H2O/dimethylacetamide at 5.degree. to give a ppt. contg. 80% 6R-I.II. Addn. of dimethylacetamide to the mother liquors followed by stirring at 10.degree. pptd. (6S)-I.II having optical purity .gtoreq.99%. The latter was treated with CaCl2 in H2O/EtOH to give Ca (6S)-folinate.

IT **58-05-9P**
RL: SPN (Synthetic preparation); **PREP (Preparation)**
(prepn. and **diastereomer** sepn. of, using polyamines)
RN 58-05-9 CAPLUS
CN L-Glutamic acid, N-[4-[[(2-amino-5-formyl-1,4,5,6,7,8-hexahydro-4-oxo-6-pteridinyl)methyl]amino]benzoyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

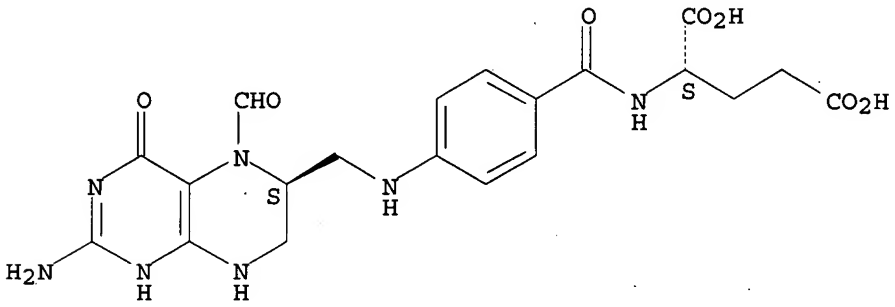


IT **68538-85-2P**, (6S)-Folinic **acid** **73951-54-9P**, (6R)-Folinic **acid** **80433-71-2P**

10/ 030,693

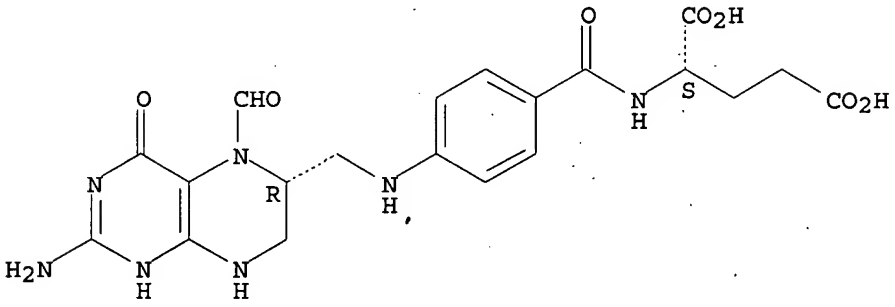
RL: SPN (Synthetic preparation); **PREP (Preparation)**
(prepn. of)
RN 68538-85-2 CAPLUS
CN L-Glutamic acid, N-[4-[[[(6S)-2-amino-5-formyl-1,4,5,6,7,8-hexahydro-4-oxo-6-pteridinyl]methyl]amino]benzoyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



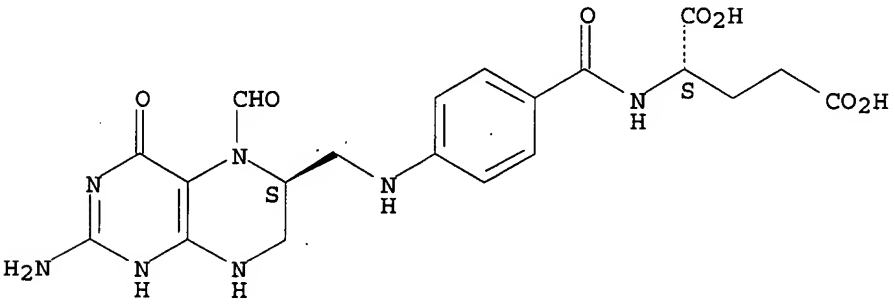
RN 73951-54-9 CAPLUS
CN L-Glutamic acid, N-[4-[[[(6R)-2-amino-5-formyl-1,4,5,6,7,8-hexahydro-4-oxo-6-pteridinyl]methyl]amino]benzoyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 80433-71-2 CAPLUS
CN L-Glutamic acid, N-[4-[[[(6S)-2-amino-5-formyl-1,4,5,6,7,8-hexahydro-4-oxo-6-pteridinyl]methyl]amino]benzoyl]-, calcium salt (1:1) (9CI) (CA INDEX NAME)

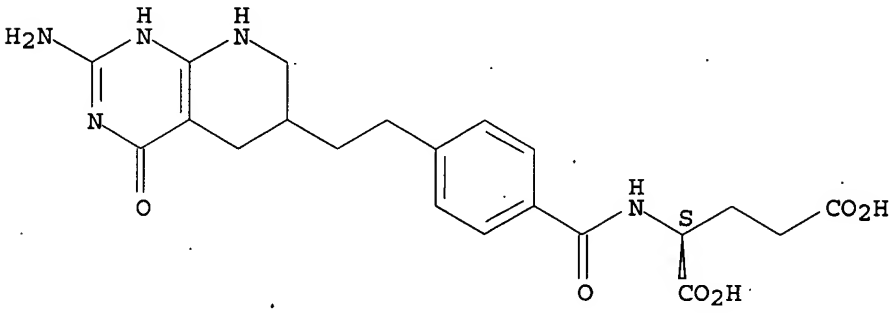
Absolute stereochemistry. Rotation (-).



Ca

L8 ANSWER 17 OF 30 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1994:31161 CAPLUS
DOCUMENT NUMBER: 120:31161
TITLE: The chemistry of DDATHF (5,10-dideaza-5,6,7,8-tetrahydrofolic **acid**) as antitumor agent
AUTHOR(S): Durucasu, Inci
CORPORATE SOURCE: Fen-Edebiyat Fak., Ataturk Univ., Erzurum, 25240, Turk.
SOURCE: Heterocycles (1993), 35(2), 1527-49
CODEN: HTCYAM; ISSN: 0385-5414
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 61 refs. Over the past 40 yr, big efforts have been devoted to the development of novel folate antimetabolites. All of the potent antifolates have reportedly been inhibitors of dihydrofolate reductase (DHFR). In 1985, E. C. Taylor and et al. reported the synthesis of DDATHF, which exhibits broad and selective antitumor activity as an inhibitor of glycinamide ribonucleotide formyltransferase (GARFT). DDATHF, a close analog of tetrahydrofolic **acid**, differs only by replacement of the 5- and 10-position nitrogen atoms by carbon. It may exist in two **diastereomeric** forms, differing in configuration at C-6. Both **diastereomers** of DDATHF are potent inhibitors of cell growth in culture. DDATHF is currently in Phase II clin. trials.
IT **95693-76-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); **PREP (Preparation)**
(prepn. and antitumor activity)
RN 95693-76-8 CAPLUS
CN L-Glutamic acid, N-[4-[2-(2-amino-1,4,5,6,7,8-hexahydro-4-oxopyrido[2,3-d]pyrimidin-6-yl)ethyl]benzoyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L8 ANSWER 18 OF 30 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1993:670915 CAPLUS
DOCUMENT NUMBER: 119:270915
TITLE: Preparation of N5-methyl- and -formylterahydrofolate **diastereomers**
INVENTOR(S): Vecchi, Giuseppe
PATENT ASSIGNEE(S): APR Applied Pharma Research S. A., Switz.
SOURCE: Eur. Pat. Appl., 5 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 537842	A2	19930421	EP 1992-203089	19921007
EP 537842	A3	19930505		
R: AT, BE, DE, DK, ES, FR, GB, IT, NL				
CH 683261	A	19940215	CH 1991-2986	19911010
US 5350850	A	19940927	US 1992-957176	19921007
CA 2080178	AA	19930411	CA 1992-2080178	19921008

PRIORITY APPLN. INFO.: CH 1991-2986 19911010

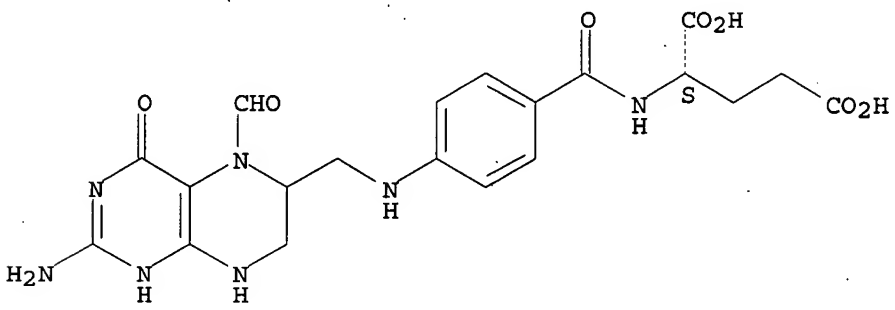
AB Title compds. were prepd. by redn. of folic **acid** (I), formylation of the product, optional redn., and pptn. as alkali or alk. earth salts. Thus, I was stirred 20 min at 90-95.degree. with NaBH4 in 20% aq. NaOH contg. EDTA, pH adjusted to .apprx.9, HCHO and NaBH4 in 0.2N NaOH added, and the whole stirred 15 min at 60.degree.. After pH adjustment (7) and filtration aq. CaCl2 was added at .apprx.0.degree. and the soln. maintained at that temp. 4-5 days to give Ca (6S)-(-)-N5-methyltetrahydrofolate.

IT **58-05-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); **PREP (Preparation)**; RACT (Reactant or reagent)
(prepn. and reaction of, in prepn. of N5-Me and -formyltetrahydrofolate **diastereomers**)

RN 58-05-9 CAPLUS

CN L-Glutamic acid, N-[4-[[(2-amino-5-formyl-1,4,5,6,7,8-hexahydro-4-oxo-6-pteridinyl)methyl]amino]benzoyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

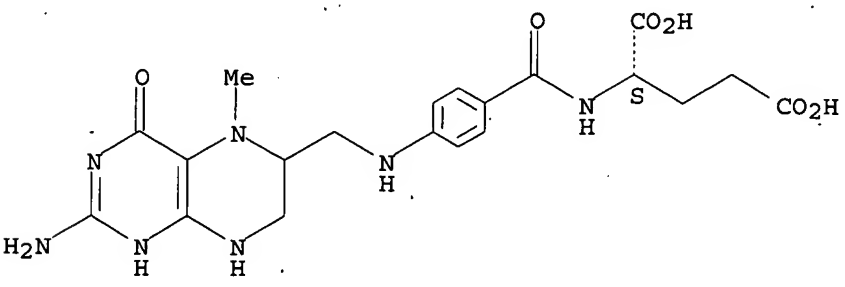


IT **134-35-0P 26560-38-3P 31690-09-2P 68538-85-2P 80433-71-2P**
RL: SPN (Synthetic preparation); **PREP (Preparation)**
(prepn. of)

RN 134-35-0 CAPLUS

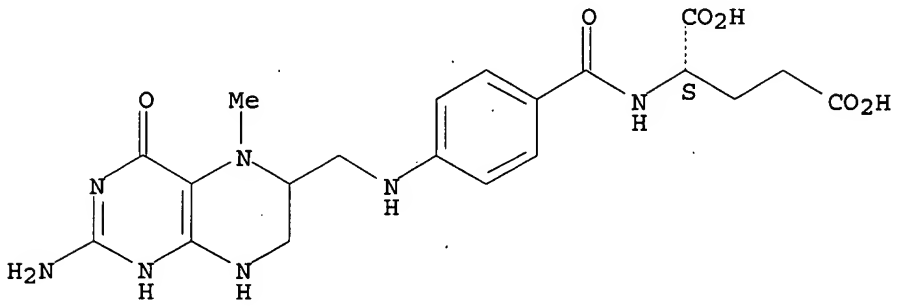
CN L-Glutamic acid, N-[4-[[(2-amino-1,4,5,6,7,8-hexahydro-5-methyl-4-oxo-6-pteridinyl)methyl]amino]benzoyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 26560-38-3 CAPLUS
CN L-Glutamic acid, N-[4-[[(2-amino-1,4,5,6,7,8-hexahydro-5-methyl-4-oxo-6-pteridinyl)methyl]amino]benzoyl]-, calcium salt (1:1) (9CI) (CA INDEX NAME)

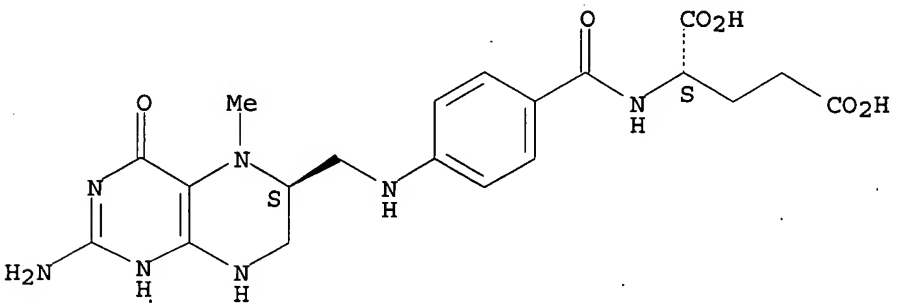
Absolute stereochemistry.



● Ca

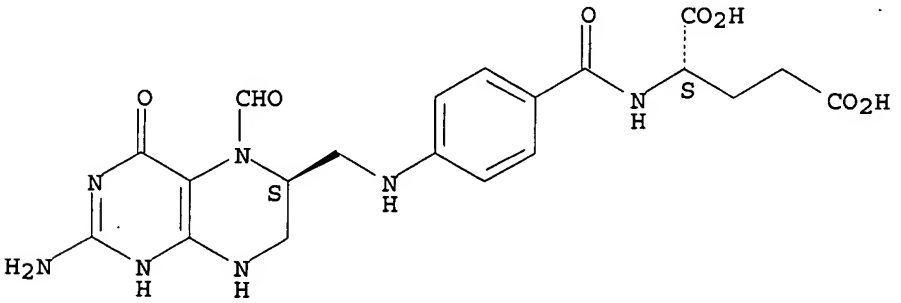
RN 31690-09-2 CAPLUS
CN L-Glutamic acid, N-[4-[[[(6S)-2-amino-1,4,5,6,7,8-hexahydro-5-methyl-4-oxo-6-pteridinyl]methyl]amino]benzoyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 68538-85-2 CAPLUS
CN L-Glutamic acid, N-[4-[[[(6S)-2-amino-5-formyl-1,4,5,6,7,8-hexahydro-4-oxo-6-pteridinyl]methyl]amino]benzoyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



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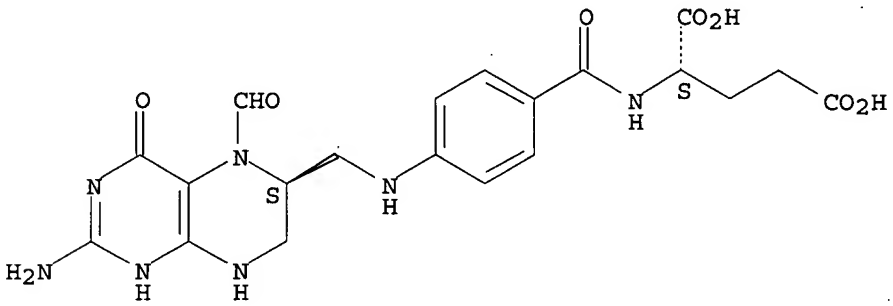
RN 80433-71-2 CAPLUS
CN L-Glutamic acid, N-[4-[[[(6S)-2-amino-5-formyl-1,4,5,6,7,8-hexahydro-4-oxo-6-pteridinyl]methyl]amino]benzoyl]-, calcium salt (1:1) (9CI) (CA INDEX NAME)

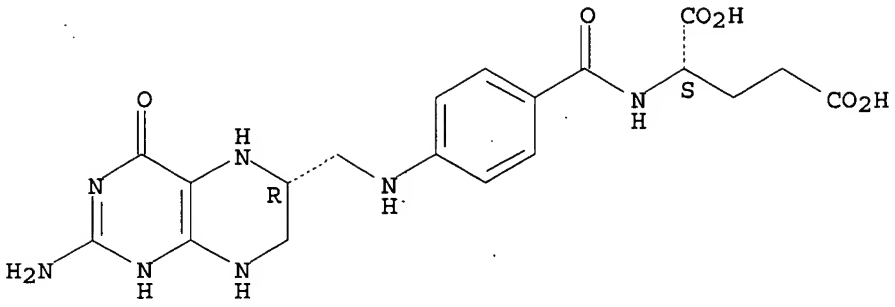
Absolute stereochemistry. Rotation (-).



O Ca

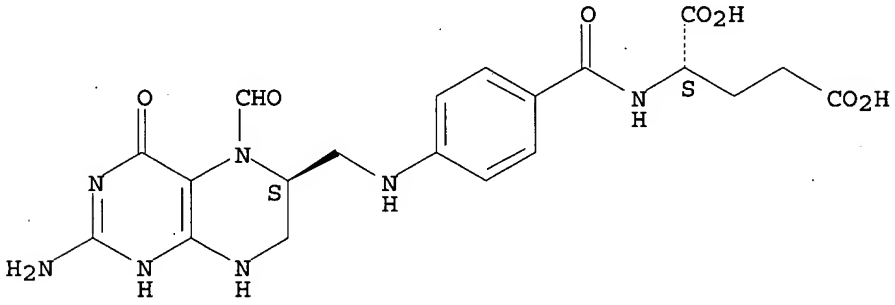
L8 ANSWER 19 OF 30 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1993:7336 CAPLUS
DOCUMENT NUMBER: 118:7336
TITLE: Asymmetric Catalysis. 67. Diastereoselective hydrogenation of folic **acid** with optically active rhodium(I)-diphosphine complexes
AUTHOR(S): Brunner, Henri; Huber, Christian
CORPORATE SOURCE: Inst. Anorg. Chem., Univ. Regensburg, Regensburg, D-8400, Germany
SOURCE: Chemische Berichte (1992), 125(9), 2085-93
CODEN: CHBEAM; ISSN: 0009-2940
DOCUMENT TYPE: Journal
LANGUAGE: German
OTHER SOURCE(S): CASREACT 118:7336
AB With immobilized Rh(I)-diphosphine catalysts supported on silica gel, the C:N bonds of the pyrazine ring of folic **acid** are reduced with H in aq. soln. to give 5,6,7,8-tetrahydrofolic **acid** (I). A mixt. of the (6S)- and (6R)-configuration is obtained at the newly formed asym. center. The unstable hydrogenation products are derivatized with (-)-menthyl chloroformate. An improved HPLC procedure for the anal. of the products has been developed. By using optically active phosphines, such as (-)-DIOP or (+)-NORPHOS as cocatalysts together with [Rh(COD)Cl]2, a **diastereomeric** excess of .ltoreq.24 % of (6S)-I is obtained.
IT **74708-38-6P**
RL: SPN (Synthetic preparation); **PREP (Preparation)**
(prepn. and derivatization of)
RN 74708-38-6 CAPLUS
CN L-Glutamic acid, N-[4-[[[(6R)-2-amino-1,4,5,6,7,8-hexahydro-4-oxo-6-pteridinyl]methyl]amino]benzoyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **80433-71-2P 111482-05-4P 115940-48-2P**
RL: SPN (Synthetic preparation); **PREP (Preparation)**
(prepn. of)
RN 80433-71-2 CAPLUS
CN L-Glutamic acid, N-[4-[[[(6S)-2-amino-5-formyl-1,4,5,6,7,8-hexahydro-4-oxo-6-pteridinyl]methyl]amino]benzoyl]-, calcium salt (1:1) (9CI) (CA INDEX NAME)

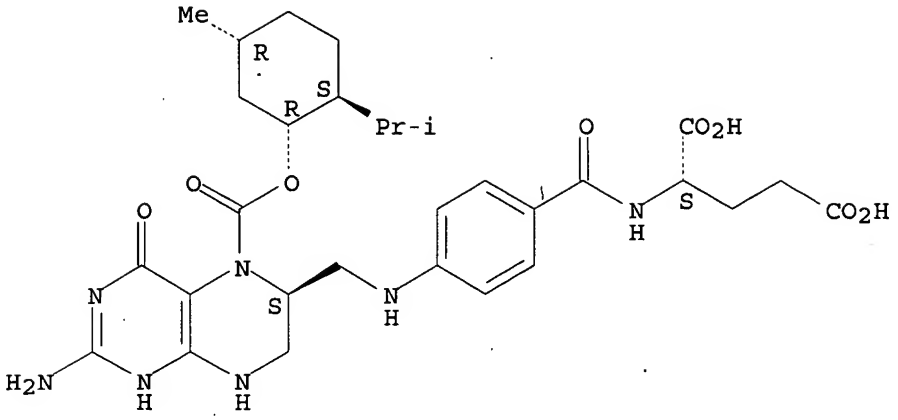
Absolute stereochemistry. Rotation (-).



● Ca

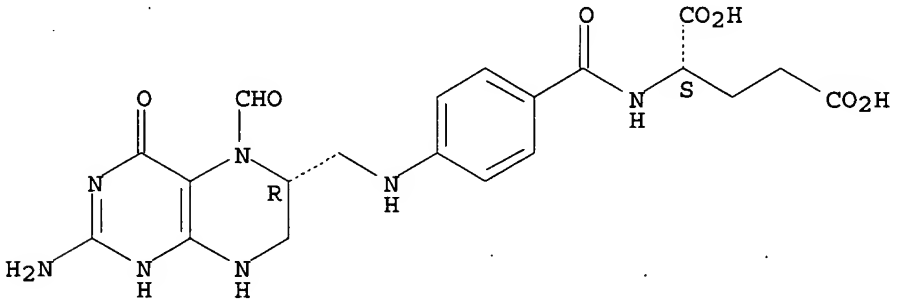
RN 111482-05-4 CAPLUS
CN L-Glutamic acid, N-[4-[[[(6S)-2-amino-1,4,5,6,7,8-hexahydro-5-[[[(1R,2S,5R)-5-methyl-2-(1-methylethyl)cyclohexyl]oxy]carbonyl]-4-oxo-6-pteridinyl]methyl]amino]benzoyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 115940-48-2 CAPLUS
CN L-Glutamic acid, N-[4-[[[(6R)-2-amino-5-formyl-1,4,5,6,7,8-hexahydro-4-oxo-6-pteridinyl]methyl]amino]benzoyl]-, calcium salt (1:1) (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



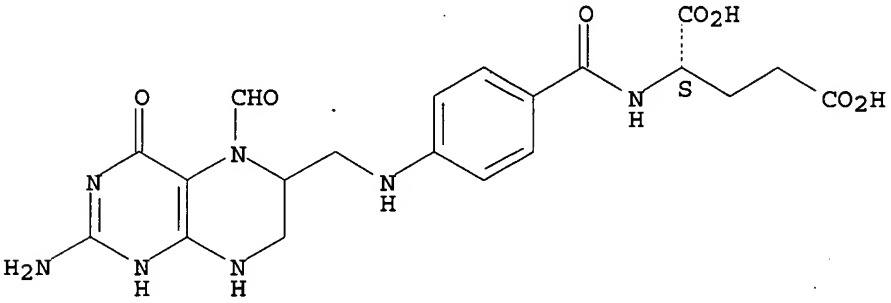
● Ca

L8 ANSWER 20 OF 30 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1992:446614 CAPLUS
DOCUMENT NUMBER: 117:46614
TITLE: Asymmetric synthesis of l-leucovorin. Part 2. NADPH regeneration by glucose dehydrogenase from Gluconobacter scleroides for l-leucovorin synthesis
AUTHOR(S): Eguchi, Tamotsu; Kuge, Yukihiro; Inoue, Kunimi; Yoshikawa, Naohiro; Mochida, Kenichi; Uwajima, Takayuki
CORPORATE SOURCE: Tokyo Res. Lab., Kyowa Hakko Kogyo Co., Ltd., Machida, 194, Japan
SOURCE: Bioscience, Biotechnology, and Biochemistry (1992), 56(5), 701-3
CODEN: BBBIEJ; ISSN: 0916-8451
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A new process for (6S)-tetrahydrofolate prodn. from dihydrofolate was designed that used dihydrofolate reductase and an NADPH regeneration system. Glucose dehydrogenase from G. scleroides KY3613 was used for recycling of the cofactor. The reaction mixt. contained 200 mM

dihydrofolate, 220 mM glucose, 2 mM NADP, 14.4 U/mL dihydrofolate reductase, and 14.4 U/mL glucose dehydrogenase, and the reaction was complete after incubation at pH 8.0 and 40.degree. for 2.5 h. With (6S)-tetrahydrofolate as the starting material, l-leucovorin was synthesized via a methenyl deriv. The purity of the l-leucovorin was 100%, and its **diastereomeric** purity was >99.5% d.e. as the (6S)-form.

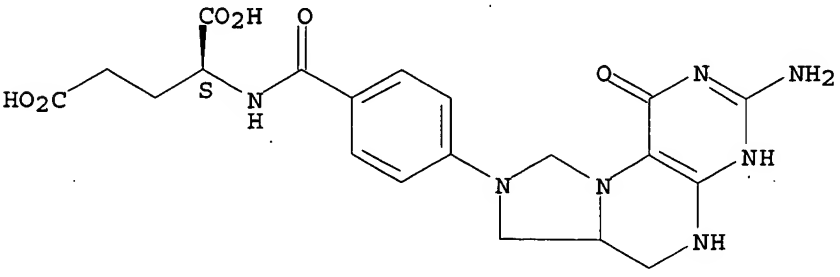
IT **58-05-9P**, l-Leucovorin
RL: BMF (Bioindustrial manufacture); BIOL (Biological study); **PREP (Preparation)**
(manuf. of, after enzymic prepn. of tetrahydrofolate, NADPH regeneration in)
RN 58-05-9 CAPLUS
CN L-Glutamic acid, N-[4-[[(2-amino-5-formyl-1,4,5,6,7,8-hexahydro-4-oxo-6-pteridinyl)methyl]amino]benzoyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **3432-99-3P**
RL: RCT (Reactant); **PREP (Preparation)**; RACT (Reactant or reagent)
(prepn. and hydrolysis of, in leucovorin manuf.)
RN 3432-99-3 CAPLUS
CN L-Glutamic acid, N-[4-(3-amino-1,2,5,6,6a,7-hexahydro-1-oxoimidazo[1,5-f]pteridin-8(9H)-yl)benzoyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **71963-69-4P**
RL: **PREP (Preparation)**
(prepn. of, by enzymic redn. of dihydrofolate, NADPH regeneration in)
RN 71963-69-4 CAPLUS
CN L-Glutamic acid, N-[4-[[[(6S)-2-amino-1,4,5,6,7,8-hexahydro-4-oxo-6-pteridinyl]methyl]amino]benzoyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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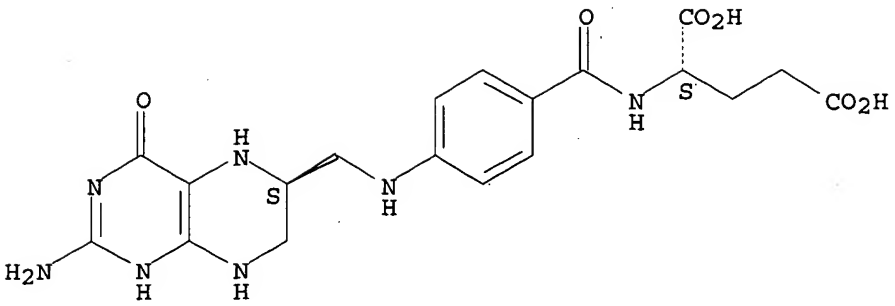
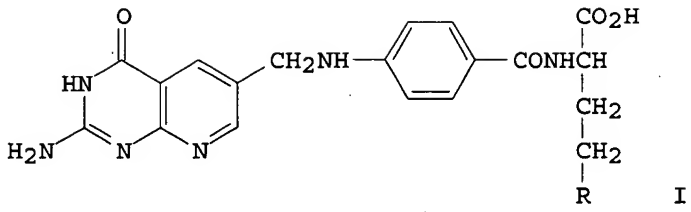


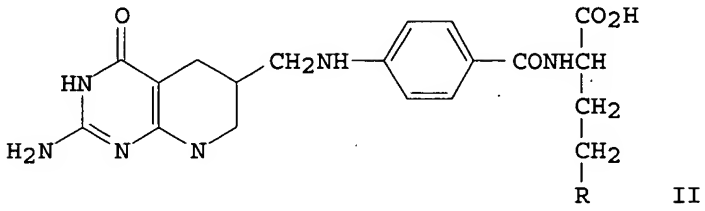
IT **9002-03-3P**, Dihydrofolate reductase
RL: **PREP (Preparation)**
(tetrahydrofolate prodn. from dihydrofolate with, NADPH regeneration in)
RN 9002-03-3 CAPLUS
CN Dehydrogenase, tetrahydrofolate (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

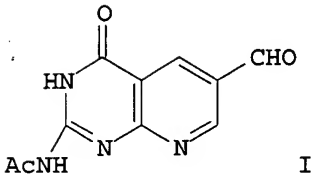
L8 ANSWER 21 OF 30 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1992:214859 CAPLUS
DOCUMENT NUMBER: 116:214859
TITLE: First use of the Taylor pteridine synthesis as a route to polyglutamate derivatives of antifolates. 46. Side chain modified 5-deazafolate and 5-deazatetrahydrofolate analogs as mammalian folylpolyglutamate synthetase and glycinamide ribonucleotide formyl transferase inhibitors: synthesis and in vitro biological evaluation
AUTHOR(S): Rosowsky, Andre; Forsch, Ronald A.; Reich, Valerie E.; Freisheim, James H.; Moran, Richard G.
CORPORATE SOURCE: Dep. Biol. Chem. Mol. Pharmacol., Harvard Med. Sch., Boston, MA, 02115, USA
SOURCE: Journal of Medicinal Chemistry (1992), 35(9), 1578-88
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 116:214859
GI



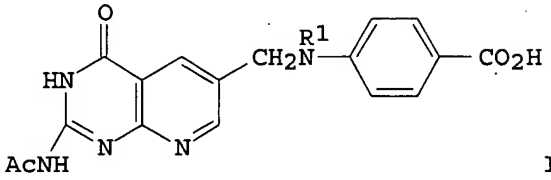
I



II



III



IV

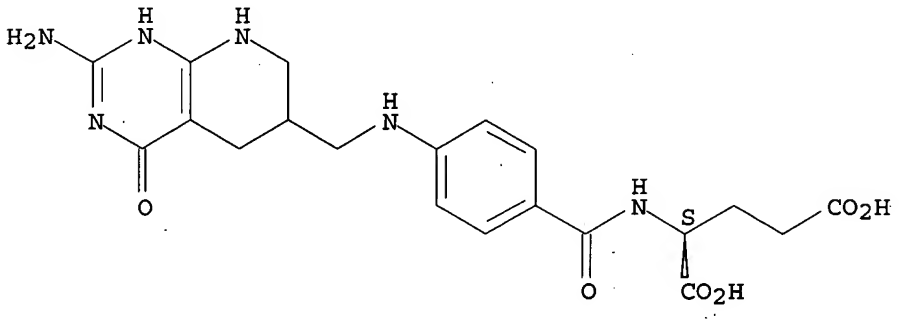
AB Title 5-deazafolate analogs I [R = SO3H, P(O)(OH)2, P(O)(OH)(OEt)] and 5-deazatetrahydrofolate (DATHF) analogs II [R = SO3H, P(O)(OH)2 P(O)(OH)(OEt), CH2NH2] were synthesized as part of a larger program direct toward inhibitors of folypolyglutamate synthetase (FPGS) as probes of the FPGS active site and as potential therapeutic agents. The tetrahydro compds. were also of interest as non-polyglutamatable inhibitors of the purine biosynthetic enzyme glycinamide ribonucleotide formyltransferase (GARFT). Thus, the reductive coupling of aldehyde III with 4-H2NC6H4CO2H in the presence of BH3.NEt3 gave 5-deazapteroic **acid** IV (R1 = H), which was formylated with HCO2H to give IV (R1 = CHO). The latter was condensed with L-homocystic **acid** by the mixed anhydride method followed by removal of the N2-acetyl and N10-formyl groups with aq. NaOH gave I (R = SO3H). The 5-deazafolate analogs were inhibitors of mouse liver FPGS, and the DATHF analogs inhibited both mouse FPGS and mouse leukemic cell GARFT. Analogs with homocysteic **acid** and monoethyl 2-amino-4-phosphonobutanoic **acid** (APBA) side chains were less active as FPGS inhibitors than those contg. an unesterified .gamma.-PO(OH)2 group, and their interaction with the enzyme was noncompetitive against variable folyl substrate. In contrast, Orn and APBA analogs obeyed competitive inhibition kinetics and were more potent, with Ki values as low as 30 nM. Comparison of the DATHF analogs as GARFT inhibitors indicated that the Orn side chain diminished activity relative to DATHF, but that the compds. with .gamma.-sulfonate or .gamma.-phosphonate substitution retained activity, with Ki values in the submicromolar range. The best GARFT inhibitor was the 5-dH4PteAPBA [II, R = P(O)(OH)2] **diastereomer** mixt., with a Ki of 47 nM vs. 65 nM for DATHF. None of the compds. showed activity against cultured WI-L2 or CEM human leukemic lymphoblasts at concns. of up to 100 .mu.M. Linking the 5-deazapteroyl moiety to these amino **acid** side chains previously found inhibitory to FPGS enhances binding of FPGs, and that neg. charged groups at the .gamma.-position of the DATHF analogs allow maintenance of GARFT inhibition. However, inefficient cellular uptake is an obstacle to the use of these potential dual inhibitors of FPGS and GARFT as therapeutic agents.

IT **115499-24-6DP**, side chain modified analogs

10/ 030,693

RL: SPN (Synthetic preparation); **PREP (Preparation)**
(prepn. and inhibition by, of folylpolyglutamate synthetase and glycinamide ribonucleotide formyltransferase)
RN 115499-24-6 CAPLUS
CN L-Glutamic acid, N-[4-[[(2-amino-1,4,5,6,7,8-hexahydro-4-oxopyrido[2,3-d]pyrimidin-6-yl)methyl]amino]benzoyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L8 ANSWER 22 OF 30 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1990:510799 CAPLUS
DOCUMENT NUMBER: 113:110799
TITLE: **Separation** of 5,10-methenyl-(6R)-, 5-formyl-(6S)-, and 5-methyl-(6S)-tetrahydrofolate mixtures via fractional crystallization
INVENTOR(S): Mueller, Hans Rudolf; Ulmann, Martin; Conti, Josef; Muerdel, Guenter
PATENT ASSIGNEE(S): Eprova A.-G., Switz.
SOURCE: Eur. Pat. Appl., 9 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 348641	A2	19900103	EP 1989-108451	19890511
EP 348641	A3	19910424		
EP 348641	B1	19950621		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
DE 3821875	C1	19900215	DE 1988-3821875	19880629
ES 2075010	T3	19951001	ES 1989-108451	19890511
DK 8902377	A	19891230	DK 1989-2377	19890516
CN 1038813	A	19900117	CN 1989-104352	19890626
CN 1032206	B	19960703		
DD 284018	A5	19901031	DD 1989-330013	19890627
FI 8903158	A	19891230	FI 1989-3158	19890628
FI 93960	B	19950315		
FI 93960	C	19950626		
NO 8902697	A	19900102	NO 1989-2697	19890628
NO 167665	B	19910819		
NO 167665	C	19911127		
AU 8937161	A1	19900104	AU 1989-37161	19890628
AU 624620	B2	19920618		
HU 50822	A2	19900328	HU 1989-3250	19890628
HU 203237	B	19910628		
ZA 8904896	A	19900328	ZA 1989-4896	19890628
CA 1339675	A1	19980217	CA 1989-604256	19890628

JP 02048577	A2	19900219	JP 1989-165487	19890629
JP 08026022	B4	19960313		
US 5006655	A	19910409	US 1989-373007	19890629

PRIORITY APPLN. INFO.: DE 1988-3821875 19880629

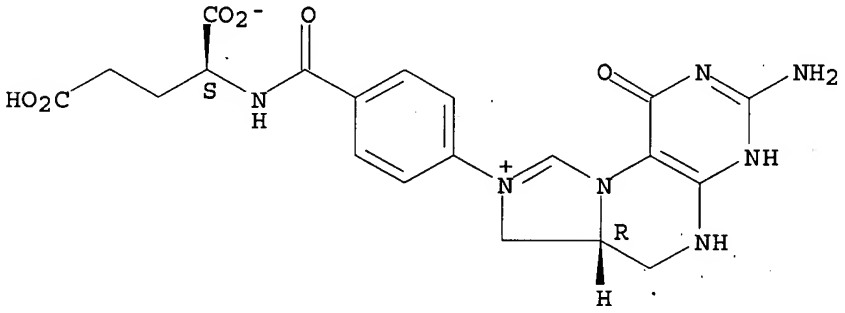
AB 5,10-Methenyl-(6R)-, 5-formyl-(6S)-, and/or 5-methyl-(6S)-tetrahydrofolic **acids** were prepd. by treatment of 5,10-methenyl-(6RS)-tetrahydrofolic **acid** with strong **acids** followed by fractional crystn. and optional hydrolysis or redn. Thus, 5,10-methenyl-(6RS)-tetrahydrofolic **acid** chloride hydrochloride dihydrate in HCO2H at 35.degree. was treated with 2N HCl followed by slow cooling to 20.degree. to give 91.5% pure 5,10-methenyl-(6R)-tetrahydrofolic **acid** chloride hydrochloride. The latter was dissolved in aq. NaOH refluxed several h at pH 5.5-6.5, cooled, and treated with aq. CaCl2 to give Ca 5-formyl-(6S)-tetrahydrofolate.

IT **7444-29-3DP**, salts with phosphoric, sulfuric, oxalic, and maleic **acid 31690-09-2DP**, magnesium complexes
31690-09-2P 68538-85-2P
RL: SPN (Synthetic preparation); **PREP (Preparation)**
(prepn. of)

RN 7444-29-3 CAPLUS

CN Imidazo[1,5-f]pteridinium, 3-amino-8-[4-[[[(1S)-1,3-dicarboxypropyl]amino]carbonyl]phenyl]-1,2,5,6,6a,7-hexahydro-1-oxo-, inner salt, (6aR)- (9CI) (CA INDEX NAME)

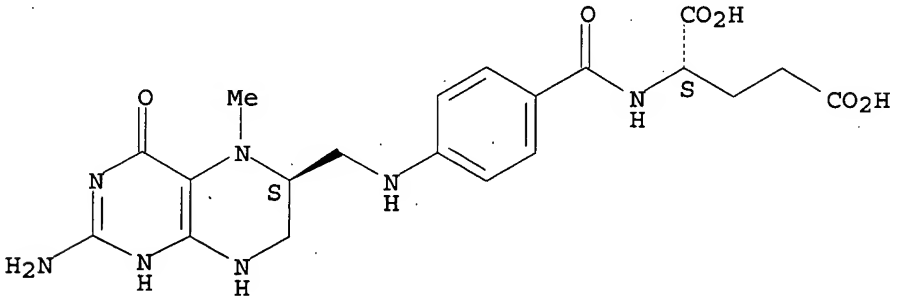
Absolute stereochemistry. Rotation (+).



RN 31690-09-2 CAPLUS

CN L-Glutamic acid, N-[4-[[[(6S)-2-amino-1,4,5,6,7,8-hexahydro-5-methyl-4-oxo-6-pteridinyl]methyl]amino]benzoyl]- (9CI) (CA INDEX NAME)

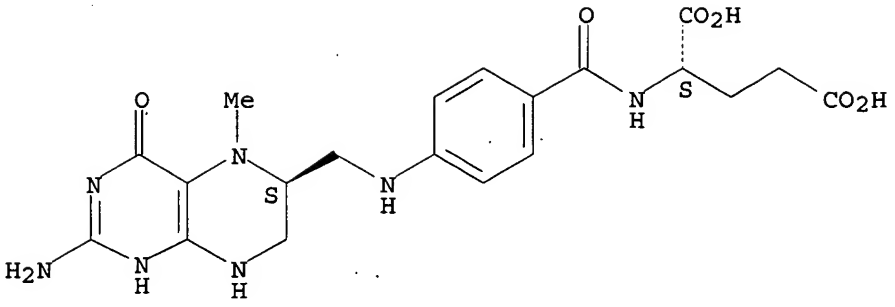
Absolute stereochemistry.



RN 31690-09-2 CAPLUS

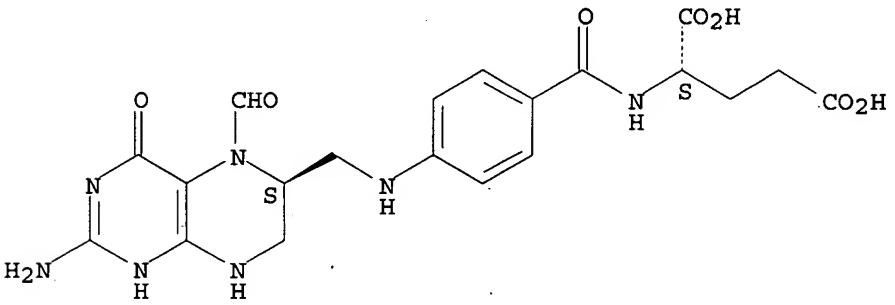
CN L-Glutamic acid, N-[4-[[[(6S)-2-amino-1,4,5,6,7,8-hexahydro-5-methyl-4-oxo-6-pteridinyl]methyl]amino]benzoyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 68538-85-2 CAPLUS
CN L-Glutamic acid, N-[4-[[[(6S)-2-amino-5-formyl-1,4,5,6,7,8-hexahydro-4-oxo-6-pteridinyl]methyl]amino]benzoyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L8 ANSWER 23 OF 30 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1989:502722 CAPLUS
DOCUMENT NUMBER: 111:102722
TITLE: Process for **separation** and isolation of (6S)-folinic **acid** from (6R,S)-folinate salts
INVENTOR(S): Mueller, Hans Rudolf; Ulmann, Martin; Conti, Josef; Muerdel, Guenter
PATENT ASSIGNEE(S): Eprova A.-G., Switz.
SOURCE: PCT Int. Appl., 19 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 8808844	A1	19881117	WO 1988-EP341	19880422
W: AU, FI, HU, JP, KR, US				
RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
CH 673459	A	19900315	CH 1987-1883	19870515
EP 293029	A1	19881130	EP 1988-200864	19880422
EP 293029	B1	19910918		
R: ES, GR				
AU 8817031	A1	19881206	AU 1988-17031	19880422
AU 603673	B2	19901122		
EP 314720	A1	19890510	EP 1988-903810	19880422
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
HU 49880	A2	19891128	HU 1988-3851	19880422

HU 201072	B	19900928			
JP 01503787	T2	19891221	JP 1988-503809		19880422
JP 08009618	B4	19960131			
AT 67498	E	19911015	AT 1988-200864		19880422
ES 2040321	T3	19931016	ES 1988-200864		19880422
DK 8802546	A	19881116	DK 1988-2546		19880509
DK 173708	B1	20010709			
CN 88102709	A	19881228	CN 1988-102709		19880511
CN 1024553	B	19940518			
ZA 8803344	A	19881228	ZA 1988-3344		19880511
DD 270073	A5	19890719	DD 1988-315677		19880511
CA 1340290	A1	19981229	CA 1988-566726		19880513
FI 8900195	A	19890113	FI 1989-195		19890113
FI 93729	B	19950215			
FI 93729	C	19950526			
US 5134235	A	19920728	US 1991-668681		19910307
US 5347005	A	19940913	US 1992-896482		19920602
US 6160116	A	20001212	US 1995-459692		19950602

PRIORITY APPLN. INFO.:

CH 1987-1883	A	19870515
EP 1988-200864	A	19880422
WO 1988-EP341	A	19880422
US 1988-294631	B1	19881223
US 1991-668681	A3	19910307
US 1992-896482	A1	19920602
US 1994-275474	B1	19940715

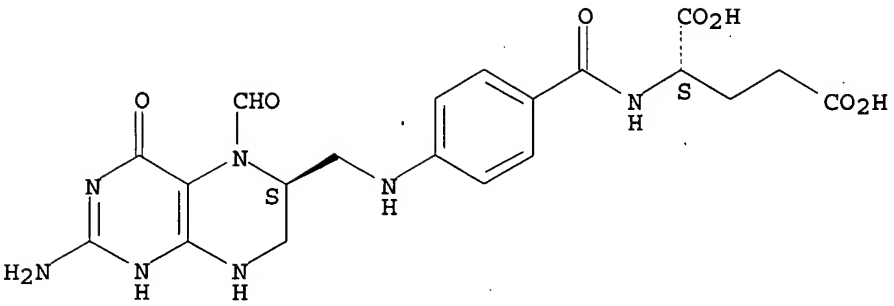
AB A method for the prepn. of (6S)-folinic **acid** or its salts comprises the recrystn. of (6R,S)-folinic **acid** alk. earth salts and, if required, the liberation of the **acid** from the alk. earth salts, and/or the conversion of the **acid** into its salts, in the presence of a base. A soln. contg. 100 g Ca (R,S)-folinate, 1 L H2O (50-60.degree.), and 12-36 g CaCl2.2H2O was adjusted to pH 10 by addn. of 25% NH4OH, and the mixt. was allowed to crystallize at 18.degree. for 18-20 h; the crystals were filtered, washed with dil. CaCl2 soln. and with EtOH to give 41 g Ca (6S)-folinate (72% yield). Ca (6S)-folinate (40g) was recrystd. by dissolving in H2O (55-60.degree.), adding 20% HCl (to pH 6.1) and 40-160 g CaCl2, and adjusting the pH at 55.degree. to 7-7.5 with NaOH; after the addn. of a seed crystal the mixt. was allowed to crystallize at 18-20.degree. for 40 h; the crystals were filtered, washed with EtOH and dried to give 30.4 g Ca (6S)-folinate (79-81% yield). Ca (6S)-folinate (10 g) was recrystd. again in the presence of 10 g CaCl2 at pH 7-7.5 to give 8 g Ca (6S)-folinate which had a soly. in H2O at 20.degree. of 0.95 g/100 mL and [.alpha.]-d20 of -15.degree. relative to the anhyd. Ca salt. Recrystn. of (6R,S)-folinate in the absence of base did not produce isomer resoln.; resoln. was obsd. by recrystn. in the presence of NaOH at pH 8.5 and recrystn. in the presence of NaOH or NH4OH at pH 10 gave a 70% and 72% optical yield, resp.

IT **68538-85-2P**
RL: **PREP (Preparation)**
(prepn. of, by hydrolysis of resolved folinate)

RN 68538-85-2 CAPLUS

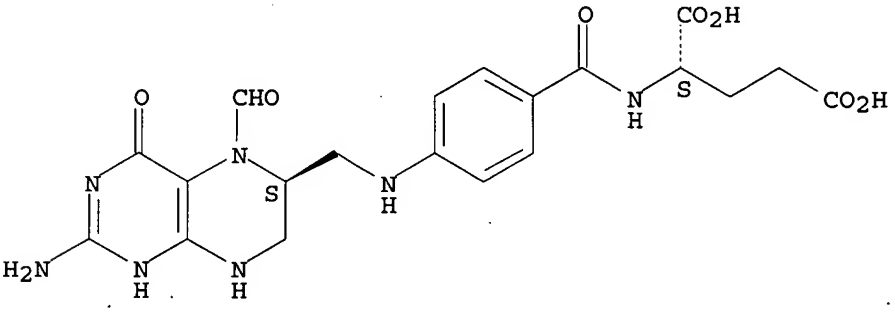
CN L-Glutamic acid, N-[4-[[[(6S)-2-amino-5-formyl-1,4,5,6,7,8-hexahydro-4-oxo-6-pteridinyl]methyl]amino]benzoyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



IT **80433-71-2P**
RL: **PREP (Preparation)**
(prepn. of, by optical resoln.)
RN 80433-71-2 CAPLUS
CN L-Glutamic acid, N-[4-[[[(6S)-2-amino-5-formyl-1,4,5,6,7,8-hexahydro-4-oxo-6-pteridinyl]methyl]amino]benzoyl]-, calcium salt (1:1) (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



● Ca

L8 ANSWER 24 OF 30 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1988:493606 CAPLUS
DOCUMENT NUMBER: 109:93606
TITLE: Preparation of leucovorin **diastereomers** as rescue agents for methotrexate cancer therapy
INVENTOR(S): Wood, Hamish Christopher Swan; Rees, Lilias; Suckling, Colin James
PATENT ASSIGNEE(S): University of Strathclyde, UK
SOURCE: Eur. Pat. Appl., 12 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 266042	A2	19880504	EP 1987-307803	19870903
EP 266042	A3	19891115		
EP 266042	B1	20030108		

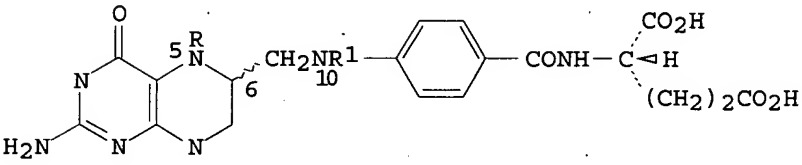
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE

AU 8777775	A1	19880331	AU 1987-77775	19870902
AU 598024	B2	19900614		
ZA 8706562	A	19890628	ZA 1987-6562	19870902
JP 63115880	A2	19880520	JP 1987-219281	19870903
JP 2844532	B2	19990106		
EP 608002	A1	19940727	EP 1994-102875	19870903
EP 608002	B1	20030115		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
AT 230746	E	20030115	AT 1987-307803	19870903
EP 1275393	A1	20030115	EP 2002-18955	19870903
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
AT 231150	E	20030215	AT 1994-102875	19870903
US 4959472	A	19900925	US 1989-403917	19890901
US 6500829	B1	20021231	US 1995-426458	19950418
US 2002198212	A1	20021226	US 2002-228820	20020827

PRIORITY APPLN. INFO.:

GB 1986-21268	A	19860903
US 1987-91989	B1	19870902
EP 1987-307803	A3	19870903
US 1989-403917	A3	19890901
US 1990-509733	B1	19900416
US 1992-869902	B1	19920415
US 1992-995350	B1	19921222
US 1993-127414	B1	19930927
US 1994-279711	B1	19940725
US 1995-426458	A1	19950418

GI



I

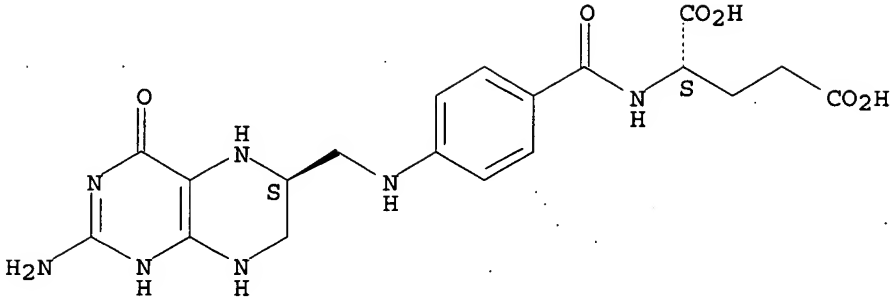
AB The (6R)- and (6S)-stereoisomers of tetrahydrofolic **acid** analogs, such as leucovorin [I, R = CHO, R1 = H (II)], were prepd. by attaching a chiral auxiliary group at N5 or N10 of the mixt. of **diastereomers** and sepg. the new pair of II **diastereomers**. The preferred chiral auxiliaries are derived from the chiral alcs. (-)-menthol, (-)-borneol, (-)-isoborneol, and D-glyceraldehyde. (6S)-II (III) is useful as a rescue agent for methotrexate cancer therapy, for treatment of folate deficiencies, and for treatment of colorectal cancer in combination with 5-fluorouracil (no data). Folic **acid** was treated with NaBH4 in aq. NaOH, followed by addn. of (-)-menthyl chloroformate and stirring 21.5 h at room temp. to give mixed **diastereomers** of I [R = (-)-menthyloxycarbonyl, R1 = H]. The **diastereomers** were sepd. by their differential soly. in BuOH, and the 6S **diastereomer** was treated with gaseous HBr in HCO2H, HSCH2CH2OH, and aq. HCl to give (6R)-tetrahydro-5,10-methenylfolic **acid** chloride. The latter was added slowly to boiling H2O, maintaining the pH at 6.5-7.0 by addn. of aq. NaOH, followed by addn. of aq. CaCl2 to give III Ca salt (1:1).

IT **71963-69-4P 74708-38-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); **PREP (Preparation)**; RACT (Reactant or reagent)
(prepn. and acylation of, by chiral chloroformates)

RN 71963-69-4 CAPLUS

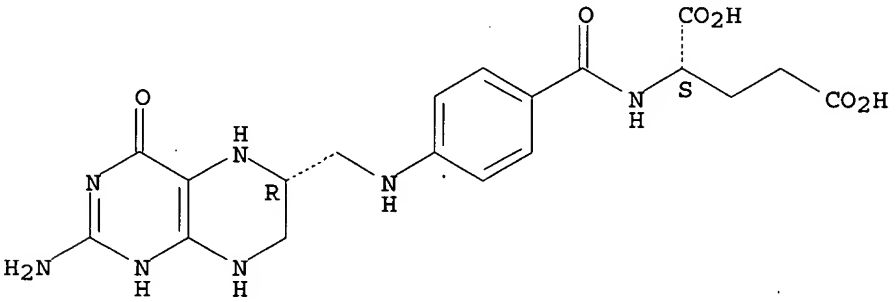
CN L-Glutamic acid, N-[4-[[[(6S)-2-amino-1,4,5,6,7,8-hexahydro-4-oxo-6-pteridinyl]methyl]amino]benzoyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



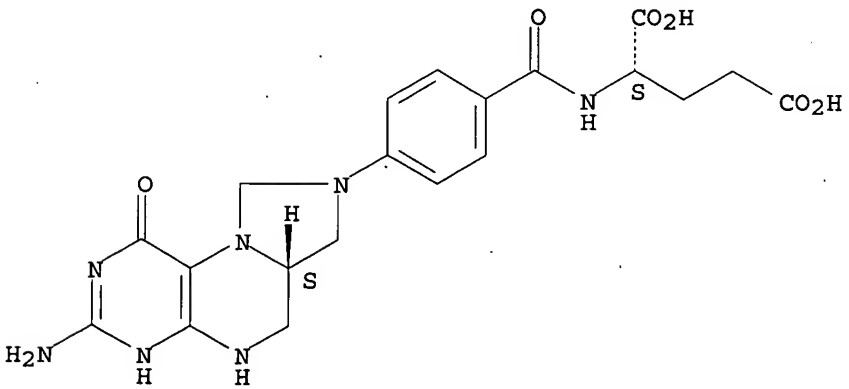
RN 74708-38-6 CAPLUS
CN L-Glutamic acid, N-[4-[[[(6R)-2-amino-1,4,5,6,7,8-hexahydro-4-oxo-6-pteridinyl]methyl]amino]benzoyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **31690-12-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); **PREP (Preparation)**; RACT (Reactant or reagent)
(prepn. and hydrolysis and cleavage of)
RN 31690-12-7 CAPLUS
CN L-Glutamic acid, N-[4-(3-amino-1,2,5,6,6a,7-hexahydro-1-oxoimidazo[1,5-f]pteridin-8(9H)-yl)benzoyl]-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



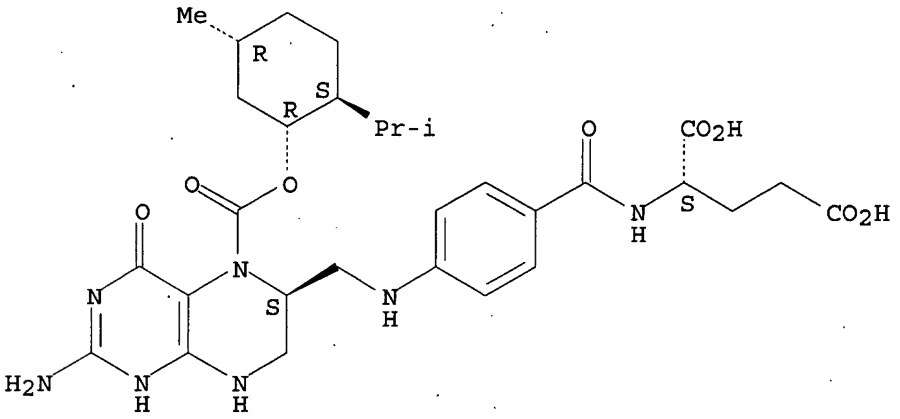
IT **111482-05-4P**
RL: PUR (Purification or recovery); SPN (Synthetic preparation); **PREP (Preparation)**

(prepn. and sepn. of, from **diastereomer**)

RN 111482-05-4 CAPLUS

CN L-Glutamic acid, N-[4-[[[(6S)-2-amino-1,4,5,6,7,8-hexahydro-5-[[[(1R,2S,5R)-5-methyl-2-(1-methylethyl)cyclohexyl]oxy]carbonyl]-4-oxo-6-pteridinyl]methyl]amino]benzoyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **31690-09-2P 115940-48-2P**

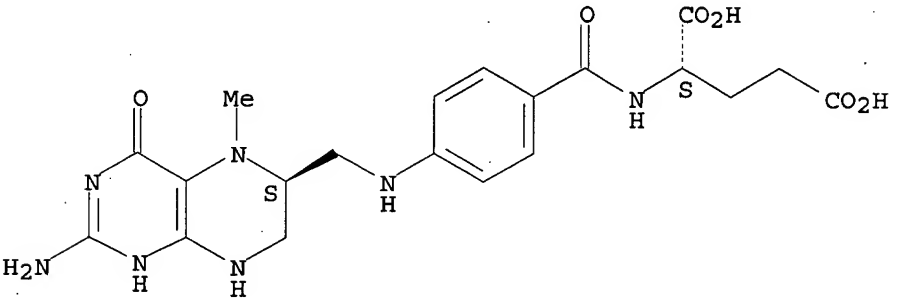
RL: SPN (Synthetic preparation); **PREP (Preparation)**

(prepn. of)

RN 31690-09-2 CAPLUS

CN L-Glutamic acid, N-[4-[[[(6S)-2-amino-1,4,5,6,7,8-hexahydro-5-methyl-4-oxo-6-pteridinyl]methyl]amino]benzoyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

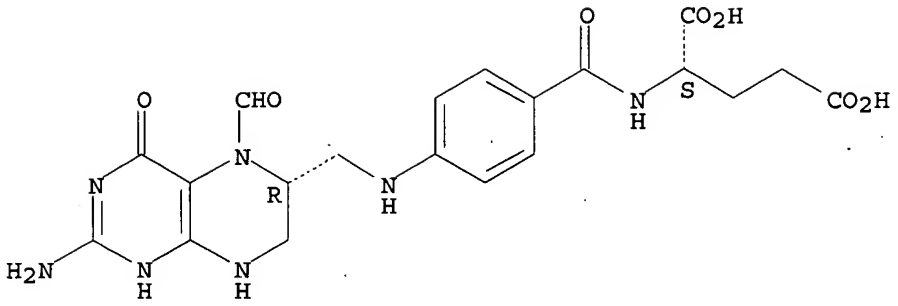


RN 115940-48-2 CAPLUS

CN L-Glutamic acid, N-[4-[[[(6R)-2-amino-5-formyl-1,4,5,6,7,8-hexahydro-4-oxo-6-pteridinyl]methyl]amino]benzoyl]-, calcium salt (1:1) (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

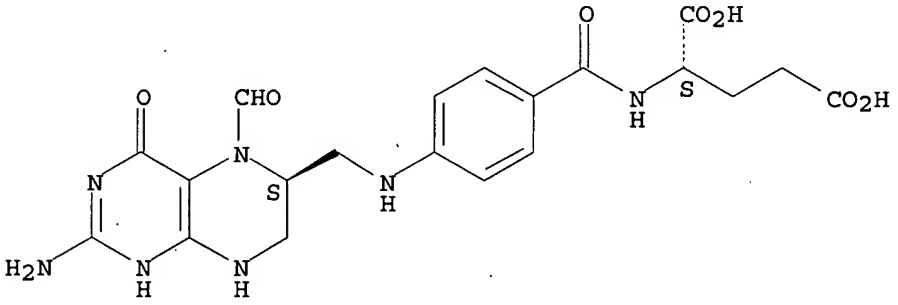
10/ 030,693



● Ca

IT **68538-85-2DP**, (S)-Leucovorin, derivs.
RL: SPN (Synthetic preparation); **PREP (Preparation)**
(prepn. of, as methotrexate rescue agents)
RN 68538-85-2 CAPLUS
CN L-Glutamic acid, N-[4-[[[(6S)-2-amino-5-formyl-1,4,5,6,7,8-hexahydro-4-oxo-6-pteridinyl]methyl]amino]benzoyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L8 ANSWER 25 OF 30 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1987:637236 CAPLUS
DOCUMENT NUMBER: 107:237236
TITLE: A simple and effective method for preparation of the 6(R)- and the 6(S)-diastereoisomers of 5-formyltetrahydrofolate (leucovorin)
AUTHOR(S): Rees, Lilias; Suckling, Colin J.; Wood, Hamish C. S.
CORPORATE SOURCE: Dep. Pure Appl. Chem., Univ. Strathclyde, Glasgow, G1 1XL, UK
SOURCE: Journal of the Chemical Society, Chemical Communications (1987), (6), 470-2
CODEN: JCCCAT; ISSN: 0022-4936
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 107:237236
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

10/ 030,693

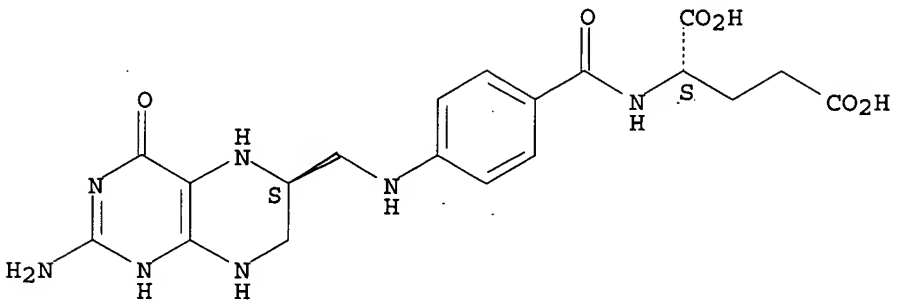
AB Folic **acid** (I) was reduced with NaBH4 and then acylated with (-)-menthyl chloroformate to give a mixt. of (6R)-tetrahydrofolate II and its (6S)-**diastereomer** (III), which were sepd. by extn. with m-BuOH. II was cyclized by HBr/HCO2H in HOAc to give 5,10-methenyltetrahydrofolate IV, which was hydrolyzed to give (6R)-5-formyltetrahydrofolate (V). The (6S)-**diastereomer** of V was prepd. similarly from III.

IT **71963-69-4P 74708-38-6P**
RL: SPN (Synthetic preparation); **PREP (Preparation)**
(prepn. and acylation with menthyl chloroformate)

RN 71963-69-4 CAPLUS

CN L-Glutamic acid, N-[4-[[[(6S)-2-amino-1,4,5,6,7,8-hexahydro-4-oxo-6-pteridinyl]methyl]amino]benzoyl]- (9CI) (CA INDEX NAME)

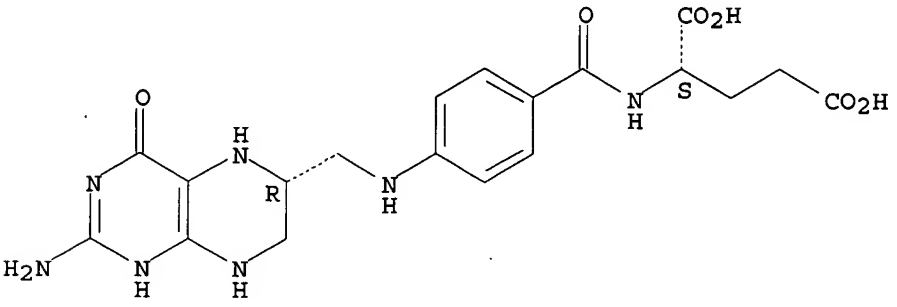
Absolute stereochemistry.



RN 74708-38-6 CAPLUS

CN L-Glutamic acid, N-[4-[[[(6R)-2-amino-1,4,5,6,7,8-hexahydro-4-oxo-6-pteridinyl]methyl]amino]benzoyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

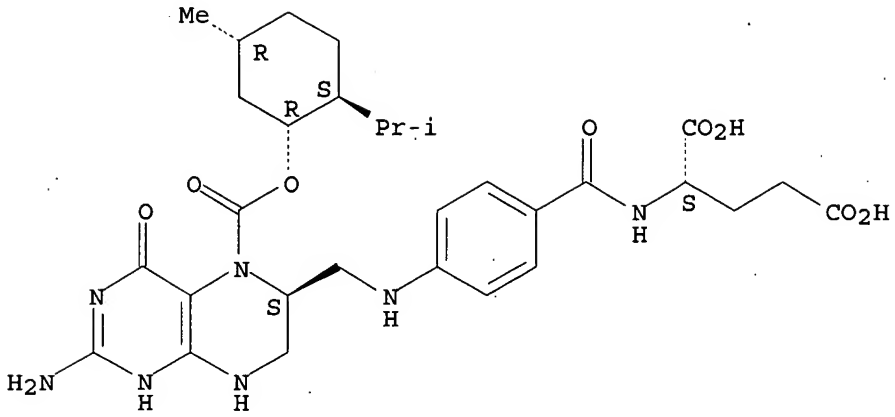


IT **111482-05-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); **PREP (Preparation)**; RACT (Reactant or reagent)
(prepn. and cyclization of)

RN 111482-05-4 CAPLUS

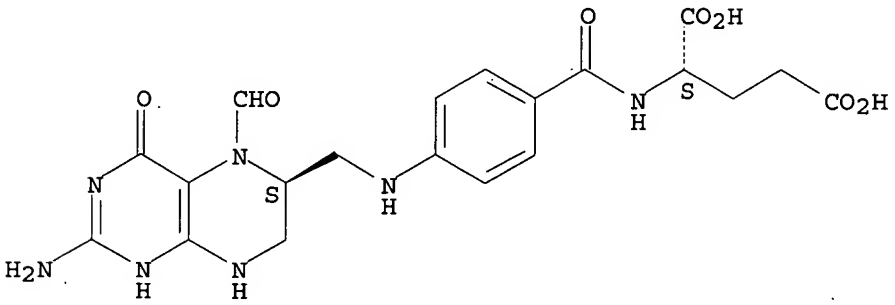
CN L-Glutamic acid, N-[4-[[[(6S)-2-amino-1,4,5,6,7,8-hexahydro-5-[[[(1R,2S,5R)-5-methyl-2-(1-methylethyl)cyclohexyl]oxy]carbonyl]-4-oxo-6-pteridinyl]methyl]amino]benzoyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



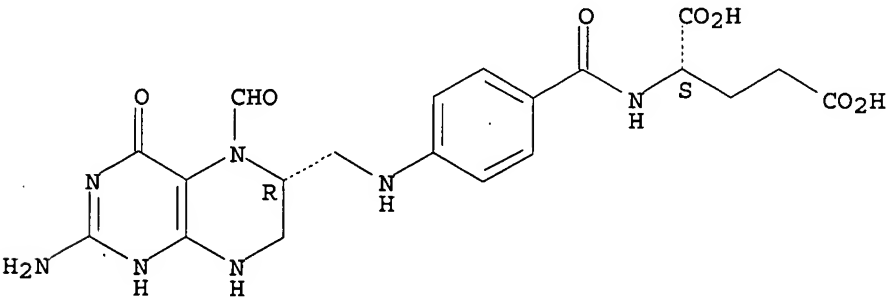
IT **68538-85-2P 73951-54-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); **PREP (Preparation)**; RACT (Reactant or reagent)
(prepn. and reductive alkylation of, with glyceraldehyde)
RN 68538-85-2 CAPLUS
CN L-Glutamic acid, N-[4-[[[(6S)-2-amino-5-formyl-1,4,5,6,7,8-hexahydro-4-oxo-6-pteridinyl]methyl]amino]benzoyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 73951-54-9 CAPLUS
CN L-Glutamic acid, N-[4-[[[(6R)-2-amino-5-formyl-1,4,5,6,7,8-hexahydro-4-oxo-6-pteridinyl]methyl]amino]benzoyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L8 ANSWER 26 OF 30 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1986:493897 CAPLUS

10/ 030,693

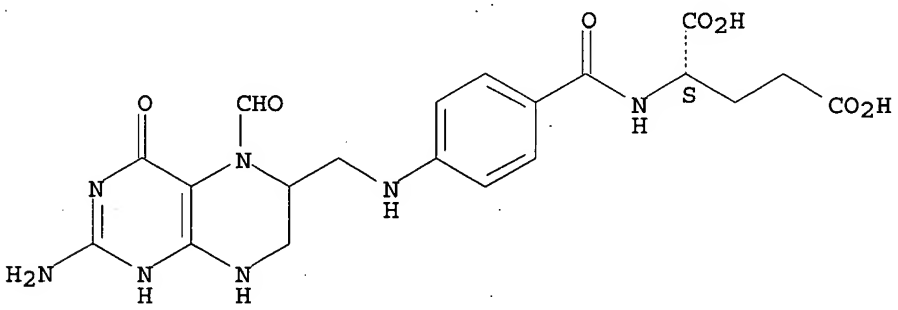
DOCUMENT NUMBER: 105:93897
TITLE: Identification of folylpoly(.gamma.-glutamate) chain length by cleavage to and **separation** of p-aminobenzoylpoly(.gamma.-glutamates)
AUTHOR(S): Shane, Barry
CORPORATE SOURCE: Dep. Nutr. Sci., Univ. California, Berkeley, CA, 94720, USA
SOURCE: Methods in Enzymology (1986), 122(Vitam. Coenzymes, Pt. G), 323-30
CODEN: MENZAU; ISSN: 0076-6879
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Folylpolyglutamates can be identified in bacterial and mammalian cells after cleavage to p-aminobenoylpooly(.gamma.-glutamates) (I) by using successive steps of **acidification**, NaBH4 redn., and Zn redn. The I obtained are converted to azo dye derivs. by the Bratton-Marshall procedure; these derivs. can be sepd. according to glutamate chain length by chromatog. on BioGel P4 or by reverse-phase HPLC.

IT **58-05-9P 134-35-0P 135-16-0P**
2800-34-2P 3432-99-3P
RL: **PREP (Preparation)**
(prepn. of)

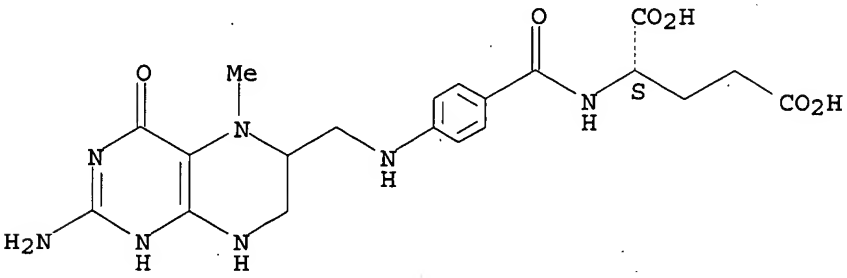
RN 58-05-9 CAPLUS
CN L-Glutamic acid, N-[4-[[(2-amino-5-formyl-1,4,5,6,7,8-hexahydro-4-oxo-6-pteridinyl)methyl]amino]benzoyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 134-35-0 CAPLUS
CN L-Glutamic acid, N-[4-[[(2-amino-1,4,5,6,7,8-hexahydro-5-methyl-4-oxo-6-pteridinyl)methyl]amino]benzoyl]- (9CI) (CA INDEX NAME)

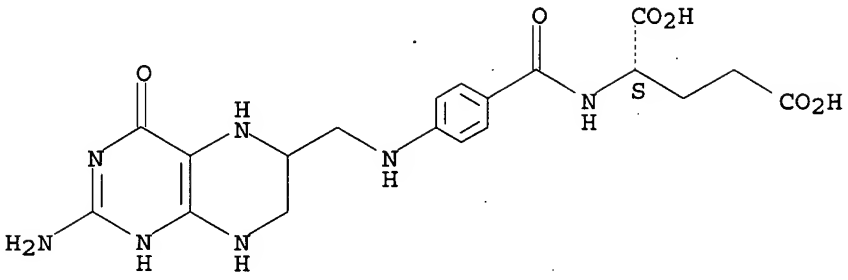
Absolute stereochemistry.



RN 135-16-0 CAPLUS
CN L-Glutamic acid, N-[4-[[(2-amino-1,4,5,6,7,8-hexahydro-4-oxo-6-pteridinyl)methyl]amino]benzoyl]- (9CI) (CA INDEX NAME)

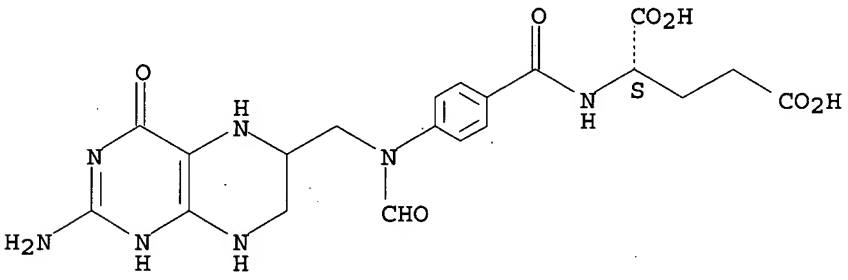
10/ 030,693

Absolute stereochemistry.



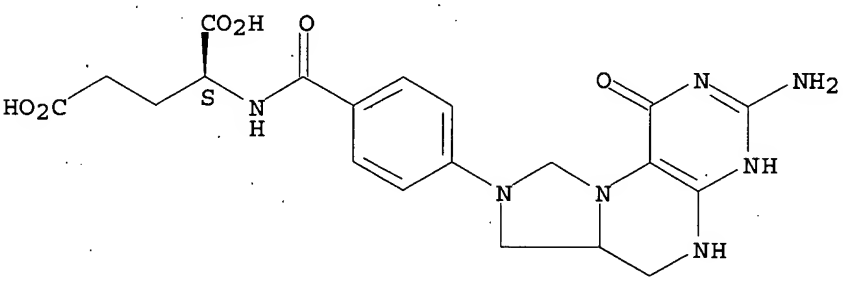
RN 2800-34-2 CAPLUS
CN L-Glutamic acid, N-[4-[[(2-amino-1,4,5,6,7,8-hexahydro-4-oxo-6-pteridinyl)methyl]formylamino]benzoyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 3432-99-3 CAPLUS
CN L-Glutamic acid, N-[4-(3-amino-1,2,5,6,6a,7-hexahydro-1-oxoimidazo[1,5-f]pteridin-8(9H)-yl)benzoyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L8 ANSWER 27 OF 30 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1986:221488 CAPLUS
DOCUMENT NUMBER: 104:221488
TITLE: Asymmetric reduction of dihydrofolate using dihydrofolate reductase and chiral boron-containing compounds
AUTHOR(S): Rees, Lilias; Valente, Edward; Suckling, Colin J.; Wood, Hamish C. S.
CORPORATE SOURCE: Dep. Pure Appl. Chem., Univ. Strathclyde, Glasgow, G1 1XL, UK
SOURCE: Tetrahedron (1986), 42(1), 117-36
CODEN: TETRAB; ISSN: 0040-4020

10/ 030,693

DOCUMENT TYPE: Journal
LANGUAGE: English

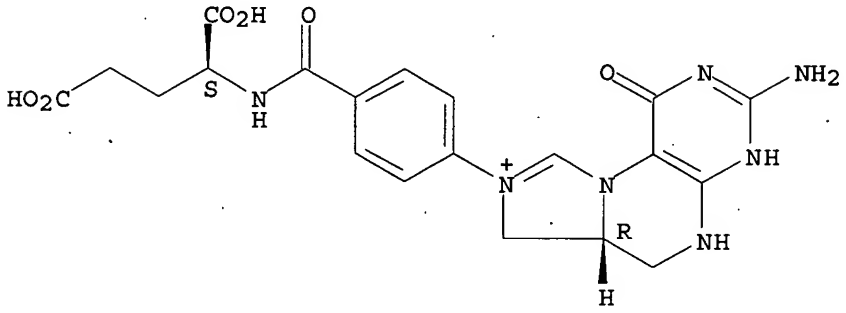
AB The redn. of dihydrofolic **acid** to chiral tetrahydrofolic **acid** was investigated by enzymic and nonenzymic means. With dihydrofolate reductase from Escherichia coli as catalyst and recycling systems for NADPH, .ltoreq.1 g of optically pure stable tetrahydrofolate derivs. was obtained. The technique makes possibile the synthesis of chiral 5-formyltetrahydrolate (leucovorin) for use in cancer rescue therapy. In contrast, although dihydrofolate was reduced by a no. of chiral boranes and borates built from amino **acids** and amino alcs., enantiomeric excesses were minimal.

IT **10360-12-0P**
RL: **PREP (Preparation)**
(prepn. and conversion to leucovorin)

RN 10360-12-0 CAPLUS

CN Imidazo[1,5-f]pteridinium, 3-amino-8-[4-[[[(1S)-1,3-dicarboxypropyl]amino]carbonyl]phenyl]-1,2,5,6,6a,7-hexahydro-1-oxo-, (6aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

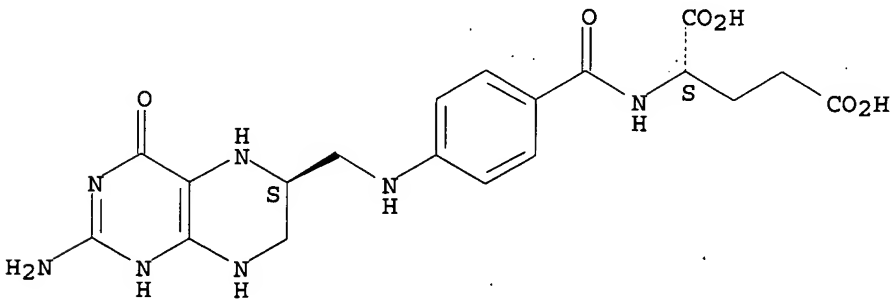


IT **71963-69-4P 80433-71-2P**
RL: **PREP (Preparation)**
(prepn. of, enzymic and nonenzymic methods for)

RN 71963-69-4 CAPLUS

CN L-Glutamic acid, N-[4-[[[(6S)-2-amino-1,4,5,6,7,8-hexahydro-4-oxo-6-pteridinyl]methyl]amino]benzoyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

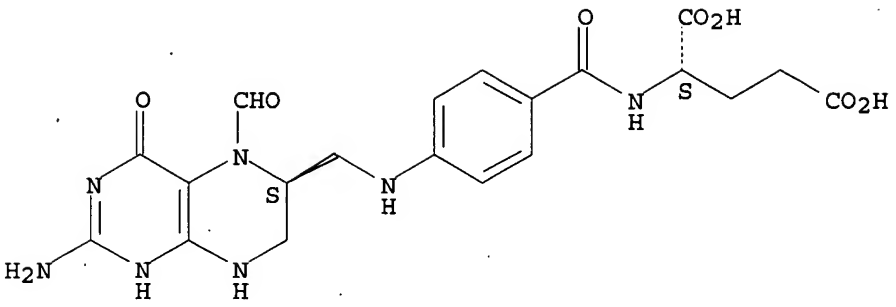


RN 80433-71-2 CAPLUS

CN L-Glutamic acid, N-[4-[[[(6S)-2-amino-5-formyl-1,4,5,6,7,8-hexahydro-4-oxo-6-pteridinyl]methyl]amino]benzoyl]-, calcium salt (1:1) (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

10/ 030,693



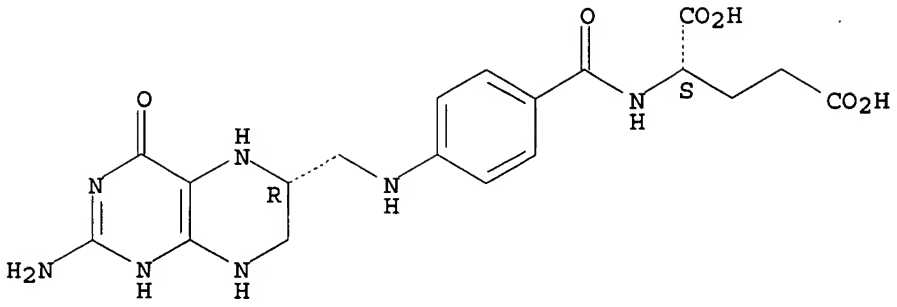
O Ca

L8 ANSWER 28 OF 30 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1986:203427 CAPLUS
DOCUMENT NUMBER: 104:203427
TITLE: Preparation of (6R)-tetrahydrofolic **acid** and (6R)-5-formyltetrahydrofolic **acid** of high stereochemical purity
AUTHOR(S): Sato, Judith K.; Newman, Edward M.; Moran, Richard G.
CORPORATE SOURCE: Div. Hematol./Oncol., Child. Hosp., Los Angeles, CA, 90027, USA
SOURCE: Analytical Biochemistry (1986), 154(2), 516-24
CODEN: ANBCA2; ISSN: 0003-2697
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Com. available 5-formyltetrahydrofolate (5-CHO-H4PteGlu) is chem. prepd. in a reaction that introduces an asym. center at the 6 carbon, and hence is the mixt. of **diastereomers** differing in chirality about this position. (6R)-5-CHO-H4PteGlu, the **diastereomer** that is not normally found in vivo, was prepd. from folic **acid**. Folic **acid** was chem. reduced and (6R)-tetrahydrofolate (H4PteGlu) was obtained from the resultant (6R,S)-H4PteGlu by enzymic consumption of the natural **diastereomer** of (6R,S)-5,10-CH2-H4PteGlu (reversibly formed from (6R,S)-H4PteGlu in the presence of formaldehyde) with Lactobacillus casei thymidylate synthase. The 5 position of purified (6R)-H4PteGlu was directly formylated in a carbodiimide-catalyzed reaction. The level of contamination of these prepns. with the corresponding 6S **diastereomers** was estd. using the binding of fluorodeoxyuridylate to thymidylate synthase promoted by folate cofactor (for H4PteGlu) and by the growth of folate requiring bacteria (for 5-CHO-H4PteGlu). Purified prepns. of (6R)-H4PteGlu promoted the binding of fluorodeoxyuridylate to L. casei thymidylate synthase (in the presence of formaldehyde) only at concns. >1000-fold higher than equiactive levels of (6S)-H4PteGlu. Likewise, the (6R)-5-CHO-H4PteGlu made by this method was 600 times less active as a growth factor for Pediococcus cerevisiae than was authentic (6S)-5-CHO-H4PteGlu. Hence, the min. stereochem. purity of these prepns. was 99.9% for (6R)-H4PteGlu and 99.8% for (6R)-5-CHO-H4PteGlu.

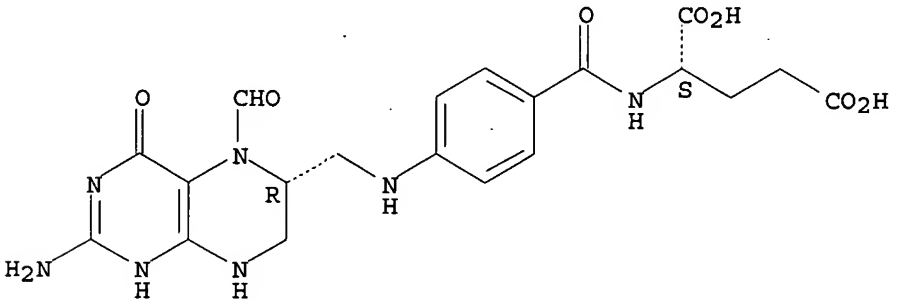
IT **74708-38-6P**
RL: SPN (Synthetic preparation); **PREP (Preparation)**
(prepn. and formalation of)
RN 74708-38-6 CAPLUS
CN L-Glutamic acid, N-[4-[[[(6R)-2-amino-1,4,5,6,7,8-hexahydro-4-oxo-6-pteridinyl]methyl]amino]benzoyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



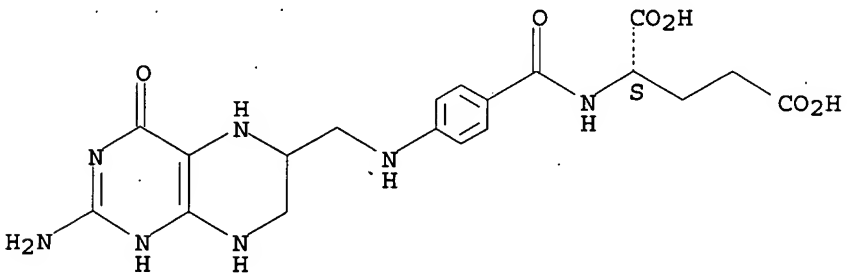
IT **73951-54-9P**
RL: **PREP (Preparation)**
(prepn. of)
RN 73951-54-9 CAPLUS
CN L-Glutamic acid, N-[4-[[[(6R)-2-amino-5-formyl-1,4,5,6,7,8-hexahydro-4-oxo-6-pteridinyl]methyl]amino]benzoyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



IT **135-16-0P**
RL: **PREP (Preparation)**
(prepn. of and natural **diastereomer** removal from)
RN 135-16-0 CAPLUS
CN L-Glutamic acid, N-[4-[[(2-amino-1,4,5,6,7,8-hexahydro-4-oxo-6-pteridinyl)methyl]amino]benzoyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L8 ANSWER 29 OF 30 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1981:204217 CAPLUS
DOCUMENT NUMBER: 94:204217
TITLE: Asymmetric reduction of L-folic **acid** at chiral electrodes
AUTHOR(S): Kwee, S.; Lund, H.

10/ 030,693

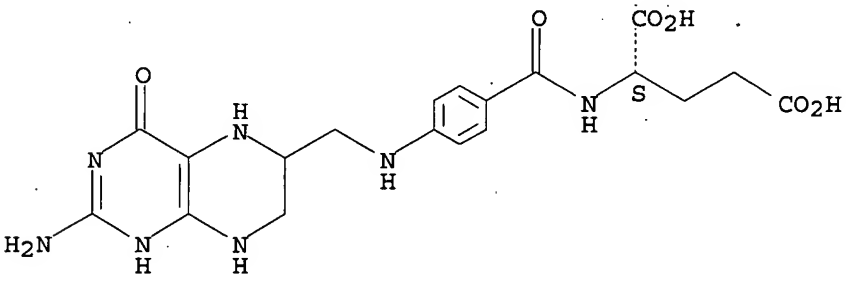
CORPORATE SOURCE: Inst. Med. Biochem., Univ. Aarhus, Aarhus, DK-8000, Den.
SOURCE: Bioelectrochemistry and Bioenergetics (1980), 7(4), 693-8
CODEN: BEBEBP; ISSN: 0302-4598
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Tetrahydrofolic **acid** (I) functions as a cofactor for a large group of enzyme-catalyzed reactions. Due to the stereoselective nature of these reactions only 1 **diastereomer** can be utilized. In the redn. of L-folic **acid** (II) to I, a 2nd asym. center is created (at C-6) yielding 2 **diastereomers**. By analogy with chem. and catalytic redns., equal amts. of l,L-I and d,L-I could be expected from the electrochem. redns. Since II is strongly adsorbed to a Hg electrode, a change of the chiral environment at the electrode might induce stereospecificity. II was reduced in the presence of small amts. of optically active compds. such as different proteins and alkaloids. At the same time the effects of a change in electrode shape and material were studied. Preliminary results showed that enantiomeric excesses .ltoreq.20% could be obtained as detd. by polarimetry and enzyme activity.

IT **135-16-0P**
RL: BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); **PREP (Preparation)**
(formation of, by folate asym. redn. at chiral electrode)

RN 135-16-0 CAPLUS
CN L-Glutamic acid, N-[4-[[(2-amino-1,4,5,6,7,8-hexahydro-4-oxo-6-pteridinyl)methyl]amino]benzoyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L8 ANSWER 30 OF 30 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1971:83399 CAPLUS
DOCUMENT NUMBER: 74:83399
TITLE: Relative configuration of N5-methyl-L-tetrahydrofolic **acid**
AUTHOR(S): Ruediger, Harold
CORPORATE SOURCE: Inst. Biochem., Univ. Koeln, Cologne, Fed. Rep. Ger.
SOURCE: FEBS Letters (1970), 11(4), 265-7
CODEN: FEBLAL; ISSN: 0014-5793
DOCUMENT TYPE: Journal
LANGUAGE: English

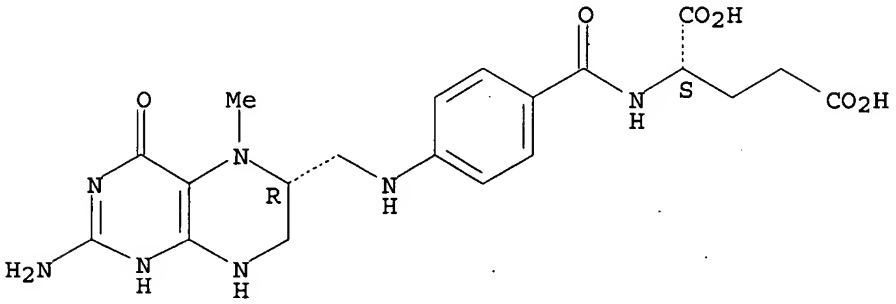
AB The optically pure isomers of dl-N5-methyltetra-hydrofolate were prepd. The resolution of **diastereomers** was performed at the level of N5, N10-methylenetetrahydrofolic **acid**. The product generated from the l-methylene deriv. was nearly inactive, in enzymic transmethylation, but this unnatural iso-mer did not inhibit transmethylation involving the natural isomer.

IT **31690-08-1P 31690-09-2P**
RL: SPN (Synthetic preparation); **PREP (Preparation)**

10/ 030,693

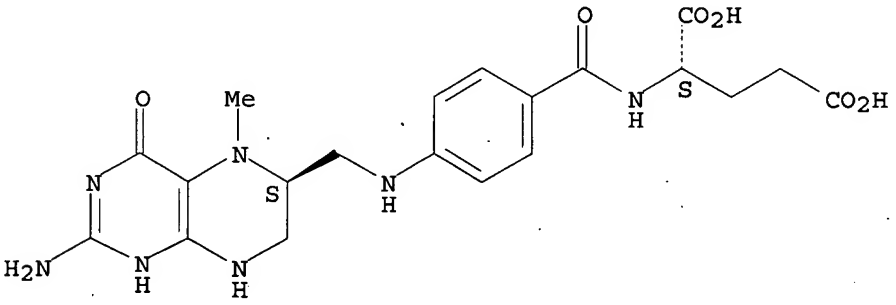
(prepn. of)
RN 31690-08-1 CAPLUS
CN L-Glutamic acid, N-[4-[[[(6R)-2-amino-1,4,5,6,7,8-hexahydro-5-methyl-4-oxo-6-pteridinyl]methyl]amino]benzoyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 31690-09-2 CAPLUS
CN L-Glutamic acid, N-[4-[[[(6S)-2-amino-1,4,5,6,7,8-hexahydro-5-methyl-4-oxo-6-pteridinyl]methyl]amino]benzoyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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(FILE 'HOME' ENTERED AT 13:15:23 ON 01 JUL 2003)

FILE 'REGISTRY' ENTERED AT 13:15:31 ON 01 JUL 2003
L1 43 S TETRAHYDROFOLIC
L2 1145 S TETRAHYDROFOLATE
L3 1180 S L1 OR L2

FILE 'CAPLUS' ENTERED AT 13:16:24 ON 01 JUL 2003
L4 571 S L3/PREP
L5 2 S L4 AND (SULPHONIC OR SULFONIC)
L6 344 S L4 AND ACID?
L7 342 S L6 NOT L5
L8 30 S L7 AND (SEPARAT? OR DIASTEREOMER?)

=> log y

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FULL ESTIMATED COST	157.84	166.89

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL

10/ 030,693

	ENTRY	SESSION
CA SUBSCRIBER PRICE	-20.83	-20.83

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